Aspects of Chromatic and Temporal Processing in Normal and Impaired Human Vision.

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Thesis submitted for the Degree of Doctor of Philosophy

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The following have been excluded at the request of the university:

Figs 1.1 & 1.2 (pg 2)

Fig 1.3 & 1.4 (pg 3)

Fig 1.6 & 1.7 (pg 6)

Fig 1.8b (pg 8)

Fig 1.9 (pg 12)

Figs 1.10 & 1.11 (pg 15)

Table 1.1 (pg 23)

Fig 1.12 (pg 26)

Fig 1.13 (pg 27)

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Abstract

A psychophysical study was made of post-receptoral processing in the human visual system. The first series of experiments investigated normal red-green opponent-colour function by means of a paradigm in which a white auxiliary field was made spatially coincident with the test field. This auxiliary field produced a deep trough in the test spectral sensitivity curve at around 580 nm, characteristic of opponent-colour processes. The efficacy of the paradigm was verified operationally by comparing thresholds for simple detection with those for colour discrimination. The paradigm was also used in measurements of field spectral sensitivity, and the upper envelope of the resulting spectrally sharpened field curves was shown to correspond in shape to the test spectral sensitivity curve. This correspondence was thought to be evidence of unitary opponent-colour processes underlying direct and adaptational measures of sensitivity, a notion which was supported by further experiments in which the test and field-envelope curves were affected similarly by the introduction of chromatic adaptation.

The paradigm was exploited in a study of chromatic and luminance function in patients with multiple sclerosis or optic neuritis. Equal losses in chromatic and luminance sensitivity were revealed, in contrast to previous studies. As a control on the procedure, two subjects with inherited red-green deficiencies were also investigated.

The response to time-varying luminance and chromatic stimuli was studied using square-wave flicker stimuli in normal subjects and patients with multiple sclerosis or optic neuritis. There was a greater reduction in luminance CFF than in chromatic CFF, but it was argued that this was a result of a general impairment in the ability of demyelinated nerve fibres to transmit high-frequency impulses.

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Chapter 1

Introduction

1 Introduction

1.1 Outline

The purpose of the research described in this thesis was to investigate, by psychophysical means, certain aspects of chromatic and temporal information processing in the human visual system. Of particular interest was the post-receptoral processing which mediates colour vision, both in the normal pathway and in subjects with certain abnormalities of the visual system, either inherited or acquired. The approach throughout this work was to develop and validate investigatory techniques for the normal visual system and then apply them to cases of impaired vision.

In the following sections, a brief review is given of the basic anatomy, spectral sensitivity, and physiology of the visual system (Sections 1.2, 1.3, and 1.4) and of abnormalities which affect colour vision (Section 1.5). Section 1.6 then sets out in detail the aims and organisation of the present work.

1.2 Anatomy of the visual system

The gross anatomy of the visual system is summarized in Figures 1.1 to 1.4. Fig. 1.1 shows the structure of the human eye in horizontal section. The structure of the human fovea as observed by Polyak (1957) is shown in Fig. 1.2. Fig. 1.3 is a schematic diagram of the ultrafine structure of the human retina, drawn by Dowling and Boycott (1966) from their electron-microscopic observations. A schematic diagram of the main neural pathways of the human visual system is shown in Fig. 1.4.

Figure 1.1 Horizontal section of the right human eye (from Rodieck, 1973).

Figure 1.2 Structure of the human fovea (from Polyak, 1957). Lower sketch shows the structural composition. Upper sketch schematizes the layers. labelled thus: Ch, choroid membrane; 1, pigment epithelium; 2, rods and cones; 4, outer nuclear layer; 5, outer plexiform layer; 6, inner nuclear layer; 7, inner plexiform layer; 8, ganglion cells; 9, optic nerve fibres. The scales indicate dimensions in μm.

Figure 1.3 Schematic diagram of the ultrafine structure of the human retina. C, cone; R, rod; MB, midget bipolar; RB, rod bipolar; FB, flat bipolar; H, horizontal cell; A, amacrine cell; MG, midget ganglion; DG, diffuse ganglion. (From Dowling and Boycott, 1966.) N.B. Kolb (1970) showed that horizontal cells have dendrites ending in cone pedicles only, whereas horizontal cell axon terminals end in rod spherules only.

Figure 1.4 Schematic diagram of the main neural pathways involved in human vision (from Willmer, 1982).

1.3 Spectral sensitivity

The spectral sensitivity of the visual system refers to its sensitivity to monochromatic radiation of varying wavelength (or frequency), which, for the human visual system, is effectively restricted to the range 350 to 750 nm. The spectral content of the light which enters the eye and the subsequent neural representation of that light undergo a number of modifications before a visual perception occurs. These modifications occur at three stages.

1.3.1 Pre-receptoral absorbance

The spectral content of the light itself is modified by the non-photolabile pigments of the ocular media. The cornea, the aqueous and vitreous humours, the lens, and the macular pigment each have specific absorbance spectra. The most important modifying influences are the lens and the macular pigment (Ruddock, 1972; Wyszecki and Stiles, 1982); their absorbance spectra are well known (see Figs. 1.5(a,b)) and can be allowed for, if necessary, when measuring the spectral response of the visual system (e.g. Moreland and Karr, 1979).

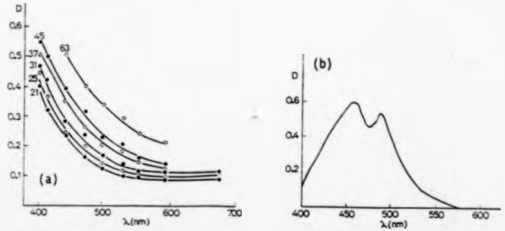


Figure 1.5 (a) The optical density, D, of living human lenses through the visible spectrum. Curves are labelled with the age of the observer.

(b) The optical density, D, of human macular pigment through the visible spectrum. (From Ruddock, 1972.)

1.3.2 Photoreceptor sensitivity

The spectral sensitivity of the pigment in an individual photoreceptor defines the probability of absorbance of a photon as a function of its frequency. It has long been understood that in the normal human retina three cone pigments of differing spectral sensitivity exist. Thomas Young's proposal in 1802 (see Brindley, 1960, for historical review) was the closest to the modern theory of trichromacy. The three fundamentals of colour vision have frequently been given hue names, but in this thesis I shall refer to them as short-wavelength (S) sensitive, medium-wavelength (M) sensitive, and long-wavelength (L) sensitive. Confirmation of trichromacy came from colour-matching experiments in which a test stimulus is matched by a maximum of three primaries (in the normal subject), one from each of the S, M, and L regions of the spectrum. The classic studies of W.D. Wright (see Wright, 1946) provided reliable quantitative colour-matching characteristics, illustrated in Fig. 1.6. The spectral sensitivity of putative individual classes of photoreceptors have been measured in vitro, by microspectrophotometry, and in vivo, by psychophysical means, the most influential method being the two-colour threshold technique of W.S. Stiles.

Microspectrophotometry. This technique allows for measurements, in vitro, of the absorbance spectra of single photoreceptors; the basic method is that a beam of monochromatic light, of variable wavelength, is passed through an isolated rod or cone outer segment, the transmittance is measured, and the absorbance then calculated. In 1964 Marks *et al*. and Brown and Wald published the first microspectrophotometric (MSP) measurements of, respectively, macaque monkey and human cones. The technique was then not accurate to more than about 20 nm, but it did provide the first non-behavioural evidence of the existence of three cone

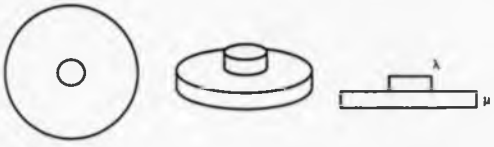
Figure 1.6 Colour matching curves showing the relative luminances of the three matching stimuli (blue, 460 nm; green, 530 nm; red, 650 nm) for the equal energy spectrum (from Wright, 1946).

Figure 1.7 Average spectral sensitivity of the four human photoreceptors, measured by microspectrophotometry (from Dartnall et al., 1983).

types, each containing a single visual pigment. (A review of MSP in its early stages was given by Liebman (1972).) Significant advances have been made since then, as listed by MacNichol et al. (1983) and Bowmaker (1984). Nonetheless, MacNichol (1986) points out that there are still limitations that are sometimes overlooked. For example, "In most MSP measurements on small outer segments (OS) the optical density (OD) measurements at wavelengths in which OD is less than 5-10% of its peak value are meaningless due to the inherent noise ..." (MacNichol, 1986, p. 1544-5). The absorbance spectra of many isolated human photoreceptors have now been measured (Dartnall et al., 1983) in addition to those of other primates (e.g. MacNichol et al., 1983; Bowmaker et al., 1983). Fig. 1.7 shows the average absorbance spectra obtained by Dartnall et al. (1983). The wavelength of peak sensitivity for L-, M-, and S-sensitive cones, and rods were, respectively, 558.4($\pm$5.2) nm, 530.8($\pm$3.5) nm, 419.0($\pm$3.6) nm, and 496.3($\pm$2.3) nm.

Two-colour threshold technique. W.S. Stiles developed the two-colour threshold technique, and in a classic series of experiments used it to derive the spectral sensitivities of S-, M-, and L-sensitive mechanisms of the human eye (see collected papers in Stiles, 1978, review by Enoch, 1972, and discussion in Wyszecki and Stiles, 1982). The aim of Stiles' work was summarized by Enoch (1972, p.538) thus: "Assuming the presence of more than one color vision mechanism, Stiles sought to isolate or reveal the individual color components by selectively reducing the sensitivity (or influence) of competing mechanisms.". The methodology used was as follows. The eye is fully adapted to a large, typically 10-deg diameter, monochromatic main or conditioning field of wavelength μ on which is presented the monochromatic test stimulus, typically 1 deg diameter, duration 200 ms and wavelength λ (see Fig. 1.8a). The increment threshold, intensity N_λ, of the test stimulus is measured for a series of different

(a)



(i) (ii) (iii)

Figure 1.8 (a) Stimulus configuration typically used to measure Stiles' π mechanisms. (i) Appearance to the subject. (ii) and (iii) Schematic representations of the stimulus configuration.

(b) The seven foveal π mechanisms found by W.S. Stiles (from Enoch, 1972).

main-field intensities, M_μ, including $M_\mu = 0$. The results can be plotted as a threshold-versus-intensity (tvi) curve. Stiles found that, with many combinations of λ and μ, tvi curves with two or three branches, each attributable to a different colour mechanism, were obtained. Two types of spectral sensitivity curve can be derived from the tvi curves. First, a field spectral sensitivity (FSS) can be obtained by fixing the test-flash wavelength (chosen to preferentially stimulate a particular colour mechanism) and measuring a series of tvi curves with different main-field wavelength. For each main-field wavelength the intensity, M_μ, required to raise the test-flash-threshold intensity, N_λ, one log unit above its value when $M_\mu = 0$ is obtained from the tvi curve. Second, a test spectral sensitivity (TSS) can be obtained by fixing the main-field wavelength and varying the test-field wavelength.

The result of Stiles' research was the description of a set of mechanisms each of which has a fixed spectral sensitivity which can be measured (within experimental constraints) by varying the wavelength of either the test field or the main field. Stiles' early work (Stiles, 1939) seemed to show that there were three mechanisms for foveal vision (and an additional one for extrafoveal vision) each of which was an independent association of photoreceptors (cones or rods). The scheme, unfortunately, proved to be more complicated, and Stiles (1953) introduced the neutral term π mechanism. Stiles found seven foveal π mechanisms, some more clearly defined than others. The π mechanisms do, however, fall into three groups according to the spectral region of peak sensitivity. These are: π_1, π_2, and π_3, S-sensitive mechanisms; π_4 and π_4', M-sensitive mechanisms; and π_5 and π_5', L-sensitive mechanisms. The spectral sensitivities of these mechanisms are shown in Fig. 1.8b.

Stiles' three main colour mechanisms, π_3 (peaking at 440 nm), π_4 (peaking at 540 nm), and π_5 (fairly flat-topped over the region 540 to 600 nm), have been shown to be well-fitted by the results of cone MSP (Bowmaker et al., 1978; Bowmaker and Dartnall, 1980) if suitable assumptions are made about the length of cones and pre-receptoral absorption losses. It has also been shown possible to express π_3, π_4, and π_5 as a linear combination of the small-field colour-matching functions (Estévez and Cavonius, 1977, Pugh and Sigel, 1978). A number of recent investigations have examined whether individual π mechanisms do represent the quantum catch of individual classes of cones; a review is given in Section 1.3.3.

To obtain spectral sensitivities by measuring a series of tvi curves is time-consuming. de Vries (1946) was probably the first to use a method of direct adjustment of main-field intensity in order to obtain FSS curves. In this method the test-flash intensity is fixed at the desired increment above absolute threshold (that is test-flash threshold when $M_\mu = 0$), and for a series of main-field wavelengths the intensity of the main field is adjusted to return the test flash to threshold. The method has been criticized (Mollon and Polden, 1977; Sigel and Pugh, 1980) but if sufficient precautions are taken to guard against transient adaptation effects then the method is fast and accurate (Foster, 1981).

1.3.3 Post-receptoral processing

Opponent-processes theories. The theory of trichromacy, outlined in Section 1.3.2, explains colour vision solely in terms of the three types of cone receptor, yet some perceptual aspects of colour vision are not easily represented in terms of such a simple model. For example, unique spectral yellow (with no tinge of red or green) can be matched perfectly by a

mixture of red and green light. In addition, adaptation to a red chromatic stimulus gives a green complementary image and vice versa. Such sensations can only be explained by postulating post-receptoral neural mechanisms in which signals from different cone types oppose each other. This type of neural mechanism is the basis for opponent-process theories, which originate from Ewald Hering. The theory was revived by Jameson and Hurvich (1955; Hurvich and Jameson, 1957; Jameson, 1972). Guth and Lodge (1973) and Ingling and Tsou (1977) developed numerically sophisticated versions of these theories. In general, such a theory usually assumes two parallel systems that process signals from the three cone mechanisms. One system is an opponent-colour system, typically signalling hue, which transmits cone signals that are combined with different signs. The other is a non-opponent system, typically signalling luminance, which transmits cone signals that are combined with the same sign. The opponent-colour or chromatic system is usually supposed to consist of two channels: the red-green channel, in which signals from L-sensitive cones oppose signals from M-sensitive cones; and a blue-yellow channel in which signals from S-sensitive cones oppose signals from both L- and M-sensitive cones. The relative responses of these channels were measured by Jameson and Hurvich (1955) using a method of hue-cancellation. Such functions, calculated for the 1931 CIE standard observer, are shown in Fig. 1.9 (curves with symbols).

The luminance or achromatic or non-opponent, system was originally postulated to consist of a single channel which combines signals from all cone types; there is controversy, however, about the size, if any, of the contribution of signals from S-sensitive cones. The relative responsivity of this system was also measured by Jameson and Hurvich (1955); the function calculated for the 1931 CIE standard observer is indicated by the solid line in Fig. 1.9.

Figure 1.9 Spectral distributions of opponent response processes for the CIE standard observer (from Hurvich and Jameson, 1962).

There has been much discussion in the literature on the properties and functional organisation of the luminance and opponent-colour systems, some details of which are reviewed in the following sections.

Post-receptoral processing revealed by psychophysical techniques. The characteristics of the chromatic, opponent-colour system and the achromatic, non-opponent system as determined psychophysically have been formulated in detail in recent years. It should be emphasized that the proposed characteristics, outlined below, relate to general psychophysically defined opponent-colour and non-opponent systems. The main properties of opponent and non-opponent processes are as follows.

i. Relative to the non-opponent system, the opponent-colour system has poorer high spatial-frequency response, or greater spatial integration (van der Horst et al., 1967; van der Horst and Bouman, 1969; Hilz and Cavonius, 1970; Granger and Heurtley, 1973; King-Smith and Carden, 1976; Sternheim et al., 1978; Stromeyer et al., 1978ab; Stromeyer and Sternheim, 1981; Mullen, 1985).

ii. Relative to the non-opponent system, the opponent-colour system has poorer high temporal-frequency response, or greater temporal integration (de Lange, 1958; Regan and Tyler, 1971; King-Smith and Carden, 1976; Kelly and van Norren, 1977; Tolhurst, 1977; Sternheim et al., 1978; Stromeyer et al., 1978ab; Sternheim et al. 1979; see also Klingaman et al., 1980; Bowen, 1981; Dain and King-Smith, 1981).

iii. The sensitivity of the non-opponent system is preferentially depressed by white (achromatic) background fields of moderate to high intensity (King-Smith and Carden, 1976; King-Smith and Kranda, 1981).

iv. Signals from S-sensitive cones are thought not to have access to the luminance system (Guth et al., 1968; Mollon and Krauskopf, 1973; Smith and Pokorny, 1975; Stromeyer et al., 1978c, 1979). A recent study by Blythe et al. (1986) (see below), however, shows that S-sensitive cones can

contribute to a luminance channel, although, as the authors recognize, their data did not indicate the size of this contribution.

By choosing stimuli according to these properties it is possible to measure, psychophysically, activity of either the opponent-colour system or the luminance system.

Test spectral sensitivities on white backgrounds. The shape of a TSS curve is determined by the mechanism or mechanisms which mediate detection of the test flash, and these mechanisms in turn are determined by the stimulus parameters as described above. A number of researchers have made use of a particular paradigm in which the test flash is relatively large, say 1-deg diameter, and of relatively long duration, say 200 ms, and the background is white and of diameter, say 10 deg. This paradigm was probably first used by Stiles and Crawford (1933), although they made their most detailed measurements using a white surround to the test field. The TSS curves they obtained, shown in Figure 1.10, have three peaks. For the foveal curves these peaks occurred in the S region of the spectrum at around 440 nm, in the M region at 538 nm, and in the L region at 602 nm (means over two subjects). Stiles and Crawford (1933) initially concluded (p. 527) that "A close connection of the three maxima at 0.44 μ, 0.54 μ and 0.60 μ, with the three mechanisms postulated by the trichromatic theory is indicated.". Stiles (1978) later explained that this original conclusion had been misleading, stating "The proposal to represent the resulting foveal spectral sensitivity as a linear combination of fixed component sensitivities was soon realized to be inconsistent with any acceptable shapes of these component curves." (see Stiles, 1978, Chapter I). Instead it has been suggested that the peaks represent activity in opponent-colour channels. Evidence leading to this suggestion is reviewed in Chapter 3.

Figure 1.10 Test spectral sensitivity for a test flash with a large white surround. Each box shows data for a different subject. (From Stiles and Crawford, 1933).

Figure 1.11 Sharpened field spectral sensitivity curves (filled symbols) compared with field spectral sensitivity of the π_4 and π_5 mechanisms (open symbols) from the same subject (from Foster, 1981).

Sharpened field spectral sensitivities. Recent investigations have shown that if the FSS curves of the L- and M-sensitive mechanisms, normally corresponding to π_5 and π_4, are measured using a paradigm which would tend to favour detection by the opponent-colour system, then the resultant FSS curves show peaks at around 530 or 605 nm. Thus Foster (1979, 1980, 1981) introduced a monochromatic 'auxiliary' field spatially coincident with the test field. In measurements of the L-sensitive mechanism he used a green auxiliary field, and in measurements of the M-sensitive mechanism he used a red auxiliary field. The resultant FSS curves were narrower than the corresponding Π mechanisms and had peak sensitivity displaced in opposite directions along the wavelength scale to around 530 nm (from 540 nm) for the M-sensitive mechanism and to around 605 nm (from around 560 nm) for the L-sensitive mechanism (see Fig 1.11). Foster referred to this displacement and narrowing as 'spectral sharpening'. He explained the effect of the spatially coincident auxiliary field in terms of the greater vulnerability of the non-opponent system, compared to the opponent-colour system, to the high spatial-frequency masking that would occur at the coincident boundaries of the test and auxiliary fields. Foster showed that reduction of test-flash duration reduced or abolished spectral sharpening, consistent with the evidence reviewed above, that the opponent-colour system has greater temporal integration than the non-opponent system. Further, spectral sharpening did not occur for the S-sensitive mechanism, consistent with evidence that S-sensitive cones input only to opponent-colour pathways in this detection task. Foster showed that the action spectrum of the process producing spectral sharpening of the L-sensitive mechanism coincides with that of the spectrally sharpened M-sensitive mechanism.

Finkelstein and Hood (1981) showed FSS curves for the L-sensitive mechanism which were spectrally sharpened in a manner analagous to that described above. In their paradigm they used a large white background

field (which would tend to favour detection by the opponent-colour system, see above) and a main field of variable wavelength, which had duration 500 ms and onset coincident with that of the test flash. The curves obtained showed a dip at around 580 nm. They were investigating the effect previously called 'cone saturation', and showed that, in fact, the effect is a result of opponent processes. They do not explicitly recognize that the temporal coincidence of the onsets of the test and main flashes would tend to cause temporal masking of the non-opponent system. In a further paper Finkelstein and Hood (1982) using the same paradigm but with a 580 nm test, obtained FSS curves which had sharp peak at around 540 nm, a dip at around 580 nm, and a secondary peak or shoulder at about 600 nm. These curves, apart from the sharp drop in sensitivity at short wavelengths, are reminiscent of those produced by Stiles and Crawford (1933) for TSS on a large white background (see above).

Spatio-temporal filters. Ruddock and his colleagues developed a paradigm designed to investigate spatial and temporal pathways in human vision (Barbur and Ruddock, 1980ab; Holliday and Ruddock, 1983); a moving test stimulus was presented on backgrounds which were modulated spatially, temporally, or both. Two spatio-temporal filters were found with properties which resemble those for single cells (see Section 1.4). Thus filter ST1 (resembling X-cells) has responses which are relatively high-frequency spatially, sustained (low pass) temporally, and opponent; whereas filter ST2 (resembling Y-cells) has responses which are relatively low-frequency spatially, transient (band pass) temporally, and non-opponent. Blythe et al. (1986) investigated the contributions from π_3 and π_5 to ST2 and to detection of a test grating alternated with an adaptation grating. The data for π_3 were similar to those for π_5 and white light, showing that S-sensitive cones can contribute to luminance channels. Interestingly, however, a TSS curve measured for test- and main-field

wavelengths which would isolate π_5 and using the main-field modulations designed to isolate ST2 (Blythe et al., 1986, Fig. 2b), was reminiscent of the sharpened L field curve obtained by Foster (1981).

What processes contribute to π mechanisms? Stiles π mechanisms have been investigated in recent years by means of tests of field additivity and silent substitution among others. These investigations are reviewed briefly here as the results are relevant to the present discussion. For the mechanisms π_1 and π_3 it was concluded (e.g. Pugh and Mollon, 1979) that neural signals pass along one pathway with two sites of attenuation, the first controlled by the S-sensitive cones alone, and the second by an opponent signal.

A similar model was arrived at for the mechanisms π_5 and π_5' by Wandell and Pugh (1980). The second site does attenuate the signal if the test flash is of long duration and if the background field is spectrally neutral with respect to the second site. These authors also postulate a second model which contains a second pathway which is controlled only by L-sensitive cones. Further, they suggest that π_5 and π_5' are not distinct mechanisms and they propose a new tvi-curve template which defines sensitivity of the L-sensitive cones. Results obtained by Reeves (1982a), however, led him to conclude that detection is never mediated by L-sensitive cones alone, but that the signal is controlled either by non-opponent or opponent sites.

For the M-sensitive mechanisms there is also controversy: Sigel and Brousseau (1982), by testing the field displacement law, concluded that detection by π_4 and π_4' is always mediated by achromatic, non-opponent pathways; whereas Reeves (1982b) tested silent substitution and claimed that detection is mediated through an opponent site. The difference here

might simply reflect the different temporal aspects of the paradigms.

1.4 Single-cell neurophysiology

The spatial and temporal characteristics of the opponent-colour system described above relate to general, psychophysically defined, opponent-colour and non-opponent systems. Such systems may reflect the activity of ensembles of retinal cells that, individually, have spatial characteristics (Gouras, 1968; de Monasterio and Gouras, 1975; de Monasterio, 1978) different from cells in some areas of visual cortex (Gouras, 1972; Dow and Gouras, 1973; Zeki, 1977). As Mollon (1982) has cautioned, the various psychophysical and electrophysiological characterizations of opponent-colour processes need not always coincide (see also Ingling, 1978, and King-Smith and Carden, 1978).

Single-cell research in primates only will be considered here, as colour vision in these animals most closely approaches that in humans. The spatial and temporal properties of retinal ganglion cells have recently been reviewed by Robson (1986). The majority of ganglion cells have receptive fields organised in a circular concentric centre-surround manner, with antagonism, or opponency, between centre and surround. There are on-centre and off-centre cells which are both sub-divided into X-, Y-, and Q-cells with different properties thus:

i. Receptive-field centre size: X-cells have smaller centres than do Y- and Q-cells; X-cells are therefore more sensitive to fine spatial frequencies.

ii. Responsivity: Q-cells have lower responsivity than do X- or Y-cells.

iii. Duration of discharge: conventionally, X-cells, with discharge remaining above the resting level for a minimum of 30 s, are termed sustained; Y- and Q-cells, with discharge returning to the resting level within 30 s, are termed transient. On a shorter time scale (less than 1 s, probably more important functionally), however, there is little difference between X- and Y-cells, and, further, there is essentially no difference between their temporal frequency responses.

iv. Spectrally-dependent opponency: in the X-cell the centre and surround receive signals from different cone classes, leading to a colour-opponent signal. In the simplest case the centre is driven by L-sensitive (or M-sensitive) cones, and the surround is driven by M-sensitive (or L-sensitive) cones. The Y-cell generally has no spectrally-dependent antagonism. The Q-cell appears to show opponency between S-sensitive-cone signals and signals from M- and L-sensitive cones.

de Monasterio (1984) has reviewed in detail the spectral signals of macaque monkey neurones. There are five main types of retinal ganglion cell. Types I, III, and IV possess the typical centre-surround field described above, whereas types II and V do not. Geniculate cells have been found which correspond to types I to IV. The spectral properties of these cells are summarized below. The following conventions are used in the summary:

i. the input to a centre or to a surround is enclosed in brackets.

ii. - indicates spectral opponency, which usually occurs between a centre and surround; spectral opponency can occur within a centre or surround, and thus double-opponency can arise.

iii. + indicates summation.

Type I:	70% are (L)-(M)	)	
	10% are (L)-(M+S)	)	spectrally opponent cells
	or (M)-(L+S)	)	
	20% are (S)-(L-M)	)	
		)	spectrally double-opponent cells
Type II	(S)-(L-M)	)	
Type III	(S+M+L)-(S+M+L)		spectrally non-opponent cells
Type IV	(S+M+L)-(S+L)		cells with opponency compressed towards spectral extremes

The type I L-M or M-L cells, which are the majority of X-cells, have sometimes been considered to mediate opponent-colour processes as found in the psychophysical measurements described above. A simple correspondence, however, does not exist between spatial and temporal properties of receptive fields and those of the psychophysically defined opponent-colour channel. For example, some cells show achromatic or colour-opponent signals according to the temporal frequency of the test stimulus (Gouras and Zrenner, 1979). Ingling and Martinez-Uriegas (1985) have shown, theoretically, that the type I L-M or M-L cell could give rise to four different signals: achromatic spatial-band pass temporal-low pass; achromatic spatial-low pass temporal-band pass; chromatic spatial-band pass temporal-band pass; and chromatic spatial-low pass temporal-low pass. Of these, the last corresponds best to the opponent-colour channel defined psychophysically, yet it is only one of a number of possible signals.

1.5 Acquired and inherited visual deficiencies

There are a number of conditions in which colour vision function is deficient. These conditions may be inherited or acquired. The present work included an investigation of acquired deficiencies arising in the demyelinating diseases multiple sclerosis (MS) and optic neuritis (ON); these are usually considered to result in red-green colour deficiencies and can also lead to other impairment in visual function. Also investigated,

for comparison, were inherited red-green deficiencies.

1.5.1 Inherited red-green deficiencies

The inherited red-green deficiencies are traditionally subdivided according to colour-matching data. Thus they can be divided into two major types: the protan type involving the L-sensitive mechanism; and the deutan type involving the M-sensitive mechanism. Both types are subdivided into two: the dichromats, who require only two primaries to match any test colour, and thus appear to possess only two cone pigments (a reduction system); and the anomalous trichromats, who require three primaries in colour matching but whose matches differ from those of normal trichromats, and thus appear to have two normal and one abnormal cone pigment (an alteration system). This classification depends on small field (2^{0}) data; for large fields the data are more complex. The substantial literature on inherited colour deficiencies has been reviewed by Hurvich (1972) and Pokorny *et al*. (1979). The tritan deficiencies, which involve the S-sensitive mechanism, and which appear to have similar forms to those of the protan and deutan deficiencies, though with a different mode of inheritance, will not be considered here. The characteristics of red-green defective vision are given in Table 1.1 (from Pokorny *et al*., 1979). Wright stressed the importance of data from subjects with inherited deficiencies to the study of colour vision - "the basic data which have to be explained by any acceptable theory of normal and defective colour vision, and their analysis may itself assist in the discovery of the underlying causes of colour blindness and even of the nature of the physiological processes involved in colour perception." (Wright, 1946, p.291).

Table 1.1 Characteristics of red-green defective vision compared with those for normal vision. From Pokorny *et al*. (1979).

[1] Plus other relative minima

[2] Neutral point

Numerous theories explaining this group of deficiencies have been proposed. One group of theories depend on the assumption that it is indeed the photopigments which are affected, with dichromacy being a reduction system and anomalous trichromacy being an alteration system. The latter theories have in common an inheritance scheme involving multiple alleles (see Pokorny et al., 1979, for review). Briefly, there are two genetic loci for the alleles controlling red-green colour vision (both of which are situated on the portion of the X chromosome which is nonhomologous with the Y chromosome). The alleles which can occupy the protan locus are hypothesized to be for normal colour vision, two (or more) forms of protanomaly (simple to extreme), and protanopia. Equivalent alleles can occupy the deutan locus. The theories differ in their explanation of the effects of the alleles. It is generally accepted that dichromacy is a reduction system in which either the M-sensitive or the L-sensitive pigment is missing. There are variations around this basic format. Wald (1966) assumed a normal cone mosaic with each cone containing one of the two remaining pigments. Vos and Walraven (1971), however, postulated a reduced cone mosaic in which only the cones which would normally contain the remaining pigments are functional. A further variation is that the abnormal gene in dichromacy encodes a photopigment either identical to the remaining normal pigment (Ruddock and Naghshineh, 1974) or nearly so (Piantanida, 1974). The reduction hypothesis in general has received support from recent MSP measurements performed on photoreceptors from the eye of a deuteranope which showed normal L-sensitive cones with no evidence of M-sensitive cones (Dartnall et al., 1983) and from molecular genetics (see below).

Anomalous trichromacy is generally accepted to be an alteration system, again with variations. Wald (1966) assumed that the anomalous pigment for protanomaly differed from that for deuteranomaly. de Vries (1948)

described the Schouten hypothesis that an anomalous pigment was common to both anomalous trichromacies; no overlap, however, is found between various estimates for the protanomalous and deuteranomalous pigments (Pokorny and Smith, 1977). Ruddock and Naghshineh (1974) suggested that the anomaly may result from an admixture of two normal photopigments in a single cone. Further, if the ratio of the pigments within a cone varies between individuals, then the range of severity of anomalous trichromacy from near normal to near dichromatic is explained. This range is evidenced by Rayleigh matching data (Willis and Farnsworth, 1952, cited in Hurvich, 1972, see Fig. 1.12), and by wavelength discrimination data (Wright, 1946, see Fig. 1.13).

Alpern and his colleagues (eg. Alpern and Moeller, 1977) proposed an alternative to the multiple allele theory involving only two alleles (for normal and defective colour vision) at each locus. Natural variation, of 7-8 nm, in the λ-max of each photopigment was supposed to account for the range from simple anomaly to dichromacy. At the protan locus the normal allele would encode for L-sensitive pigment, whereas the defective allele would encode for M-sensitive pigment. At the deutan locus the normal allele would encode for M-sensitive pigment whereas the defective allele would encode for L-sensitive pigment. Thus a protan would have an allele for M-sensitive pigment at both loci: if the λ-max of the two M-sensitive pigments were similar then protanopia would result; if far apart then the individual would be protanomalous. The total range of 7-8 nm in the λ-max, however, is insufficient to explain the greater incidence in the population of anomaly than of dichromacy (see discussion in Pokorny et al., 1979).

Of relevance to this debate is the recent work of Nathans and his colleagues on the molecular genetics of human colour vision. In colour-normal males (Nathans et al., 1986a) there was one L gene (gene

Figure 1.12 Rayleigh matching data, showing the range from normal (N) through protanomaly to protanopia (P) and through deuteranomaly to deuteranopia (D). U denotes subjects unclassified by other colour vision tests (from Hurvich, 1972).

Figure 1.13 Wavelength discrimination curves showing the range of severity of impairment in anomalous trichromats from near normal to near dichromatic: (a) data for protanomalous observers; (b) data for deuteranomalous observers. (From Pokorny et al., 1979, after Wright, 1946.)

governing the L-sensitive pigment) but variation in the number of M genes. This was explained by the high similarity of the M and L genes and their adjacent positions on the X chromosome; misalignment of genetic material could therefore occur during meiosis which in turn could lead to unequal crossing over in the intergenic region resulting in a chromosome with more than one M gene. Nathans et al. (1986b) investigated dichromats and anomalous trichromats (simple to extreme) and proposed unequal crossing over in the intragenic region to explain the range of L/M hybrid genes which were found; the ratio of L/M genetic material in the region encoding for spectral sensitivity correlated with Rayleigh match performance; further, dichromats had either only L or only M genes, or one normal gene (L or M) plus a hybrid gene in which the ratio of L/M genetic material was such that the pigment would have identical or very similar spectral sensitivity to that of the pigment produced by the normal gene.

Hurvich and Jameson (1962; Hurvich, 1972) postulated a theory of defective colour vision in terms of deficiencies in the opponent-colour system in addition to possible changes in photopigment absorption spectra. Thus a dichromat would have three photopigments (which may or may not be normal) but no red-green opponency (i.e. a collapse system). Hurvich and Jameson believe that the dichromat's perception of 'white' predicates three cone pigments. (The data from MSP and molecular genetics, cited above, however, contradict this part of the theory; see also Section 6.1.1.) Anomalous trichromats would have three photopigments all of which (in the original theory) would be abnormal, and varying degrees of reduction in red-green opponency; the latter would explain the range in anomalous visual behaviour mentioned above. Reduction in red-green opponency with no alteration of the photopigments was postulated to explain the data for 'normal' trichromats who have normal midpoints on the Rayleigh match but extended ranges.

1.5.2 Multiple sclerosis and optic neuritis

Multiple sclerosis (MS) is one of the demyelinating diseases (see Waxman, 1983, for review). Optic neuritis (ON) occurs at some stage in the course of the disease in about 70% of MS patients; additionally, of patients who present initially with ON, about 70% will go on to develop MS (Perkin and Rose, 1979). Interestingly, at post mortem 100% of MS patients investigated had lesions in the optic pathways (Lumsden, 1970). In view of the close relationship between ON and MS, the two will be considered together for the present work. A typical attack of ON starts with pain in the affected eye, quickly followed by loss of vision which may or may not be complete, and which usually consists of a central scotoma. Both acuity and colour vision can return to normal in a few weeks. As the disease progresses accompanied by more frequent relapses, there is often residual visual loss in the remission phase. Differential diagnosis of ON has been described by Heron (1986). Studies on the pathogenesis of ON have been reviewed by McDonald (1986).

Processing of visual information, measured psychophysically, is often impaired in subjects with MS or ON or both (Foster, 1986; Hess and Plant, 1986). The next section reviews some of these data.

Luminance threshold. Abnormally raised luminance thresholds have been shown in certain patients with previous retrobulbar neuritis (RBN) (Burde and Gallin, 1975; Harms, 1976). Further, Harms (1976) noted that variability in luminance threshold was abnormal in certain patients recovering from RBN. Patterson *et al.* (1980) found significantly raised luminance thresholds at high background luminance levels in a selected group of patients with MS who had suffered no previous visual symptoms in the eye tested, although all had subclinical optic neuropathy as evidenced

by visual field defects. The authors had preselected patients who showed increased variability of luminance threshold; threshold variability in normal subjects remained substantially constant with increasing background luminance, whereas, for the MS patients, variability increased rapidly. Patterson et al. (1980) suggested that either ephaptic transmission (Rasminsky, 1978), or intermittent conduction block (Rasminsky and Sears, 1972), could be the underlying cause of this variability.

Colour discrimination. Patients recovering from ON often report that colours look 'washed out' or desaturated (Burde and Gallin, 1975; Glaser, 1976), and a recent report by a patient with ON gives a detailed account of the changing nature of such effects (MacKarell, 1986). These subjective impressions are paralleled by a loss in colour discrimination, as measured with the 100-Hue Test (Cox, 1961a; Griffin and Wray, 1978; Verriest, 1963), and by wavelength discrimination (Cox, 1961b). Acquired colour deficiencies have been classified according to the axis of major discrimination loss (Verriest, 1963). In MS and ON the loss is generally reported to be of a red-green type, or, specifically, a Verriest Type II acquired red-green defect, but this is not always so (e.g. Ohta, 1970, cited in Pokorny et al., 1979).

Colour mechanisms The colour mechanisms of the eye have been measured in acquired deficiencies by Marré (see Marré, 1979,) using Wald's technique of selective chromatic adaptation (Wald, 1966). Marré found reduction in sensitivity of all three colour mechanisms in patients with ON. Wald's technique, in which a TSS curve for each colour mechanism is obtained on a bright broadband chromatic main field, is related to Stile's two-colour threshold technique (Section 1.3.2) in which both test and main fields are monochromatic. Moreland et al. (1977; Maione et al. 1978) developed a variation of Stiles' technique for clinical investigations, which could be

used in the study of colour vision deficiencies in MS and ON. Their technique consisted of a monochromatic test field which was superimposed on a monochromatic main field, which in turn was superimposed on a broadband chromatic adaptation field. FSS curves were obtained by the method of direct field adjustment. The technique employs moderate intensities.

Opponent-colour and luminance systems. Acquired colour deficiencies have also been classified in terms of post-receptoral processes (Pokorny et al., 1979). Some data suggest that in MS and ON, chromatic function may suffer more severe impairment than luminance function. The data of Fallowfield and Krauskopf (1984) indicate a selective loss of chromatic sensitivity in patients with MS or ON; their method, however, is subject to criticism (see Section 7.3.3). Mullen and Plant (1986) also found that, on average, patients with ON, or MS and ON, have more severely impaired chromatic sensitivity, but some individual patients showed an equal loss of chromatic and luminance sensitivity.

Other studies have indicated that luminance function may be the more severely impaired. Alvarez et al. (1982) presented averaged data for detection of 1-Hz and 25-Hz flickering test fields on a large white background field. Patients with RBN showed a loss of sensitivity for both paradigms but the greater loss was for 25 Hz flicker, indicating a more severe impairment for luminance than for chromatic vision.

There are two explanations of the different data obtained. One is that results may not be directly comparable because methods differ between studies. The second explanation is that there are indeed different types of impairment in the patients (Alvarez and King-Smith, 1984). These points are discussed further in Section 7.3.3.

Temporal processing: two-flash resolution. Two-flash resolution has been used to indicate abnormal temporal resolution in MS patients with previous RBN (Galvin et al., 1976a,b) and in MS patients without previous RBN (Galvin et al., 1977). The paradigm is complicated, and factors such as total luminance, total duration, and spatial frequency of the stimuli have been shown to influence performance (Kietzman and Sutton, 1968; Boynton, 1972). Abnormal two-flash resolution found in MS patients has, however, been shown not to depend simply on raised luminance thresholds (Patterson et al., 1981). Galvin et al., (1977) reported that patients with advanced definite MS and previous visual involvement showed significantly poorer foveal two-flash resolution than did patients with less advanced MS with or without visual involvement.

Temporal processing: perceptual latency. This is a psychophysical method of estimating abnormal increases in the conduction velocity of neurones in the visual pathways. Abnormalities in perceptual latency for an extrafoveal site of one eye relative to the fovea of the other have been shown in patients who had experienced a previous attack of RBN and in some patients with spinal MS (Heron et al., 1974; Regan et al., 1976; Galvin et al., 1976a). Moreover Regan et al. (1976) derived the perceptual delay between the fovea and a parafoveal site for single eyes of patients with spinal MS, and showed that there was often an abnormal delay between sites in the same eye. As Regan et al. (1976) pointed out, a delay between two sites in the same eye could occur either if demyelination was patchy or of a different degree for different sites.

Temporal processing: critical flicker fusion. Patients with MS have been reported to have abnormally lowered critical flicker fusion (CFF) for luminance flicker (Titcombe and Willison, 1961; Daley et al., 1979). The classic Ferry-Porter law describes how the value of CFF depends

approximately on the intensity of the stimuli; the shape of the de Lange attenuation characteristic is also affected by mean luminance of the stimuli (de Lange, 1958; Roufs, 1972). The abnormal results given by MS patients, however, are not a simple consequence of abnormal luminance thresholds (Patterson et al., 1981).

1.6 Aims and Organisation

This thesis investigates a number of issues concerning the processing of chromatic and temporal stimuli in the normal and impaired visual system. In Chapters 3 to 5 an assessment is made of the improvement in isolation of the opponent-colour system by means of a paradigm which combines two critical stimulus properties (a white background and an auxiliary field spatially coincident with the test field, Section 1.3.3). The rationale for the use of this paradigm, and the extent of the resultant improvement in isolation of the opponent-colour system in measurements of TSS, are described in Chapter 3. In Chapter 4 the efficacy of the same paradigm in isolating the opponent-colour system in measurements of FSS is assessed. The question of whether unitary opponent-processes mediate detection both in direct measures of sensitivity (TSS) and in measures of adaptational sensitivity (FSS) is discussed in Chapter 5. This hypothesis is tested by modifying the paradigm and comparing the resultant changes in TSS and FSS.

The remaining experimental chapters contain a study of two groups of subjects with impaired vision. In Chapter 6 red-green dichromacy is examined using the paradigm mentioned above to help assess the relative contributions of receptoral and post-receptoral abnormalities. Results from a subject with MS and ON are also presented in Chapter 6 to help resolve the question of the selectivity, or otherwise, of chromatic losses

in demyelinating disease. In Chapter 7, the paradigm is modified for clinical assessment of a group of patients with MS or ON or both. In Chapter 8 the temporal aspects of the processing of chromatic and luminance information are considered. A linear relationship between chromatic and luminance CFF was found for normal subjects, and this relationship was found to change significantly in patients with MS or ON or both.

Chapter 2

Methods

2 Methods

2.1 Introduction

The experiments which were carried out fall into two broad groups with different apparatus and procedures for each. For experiments on spectral sensitivities of small numbers of subjects with (a) normal vision, (b) inherited abnormalities of the visual system, and (c) abnormalities of the visual system resulting from disease, a Maxwellian-view system (see Westheimer, 1966) supplied the stimuli. Whereas experimental observations made with a Maxwellian-view system by the methods described below are simple for a practised subject (and in general observers can become proficient after one or two practice sessions) it would be unlikely that unpractised subjects would make reliable observations with this system. As the intention for the clinical aspect of this research was to test large numbers of patients with either MS, or ON, or both, and an equal number of unpractised control subjects, a system was required which would allow these subjects to be tested easily and in comfortable conditions. These requirements were realized in a special purpose visual perimeter.

2.2 Maxwellian-view system

2.2.1 Apparatus

A schematic diagram of the four-channel Maxwellian-view system is shown in Fig. 2.1. The intensities of channels 1, 2, and 3 could be varied independently; the optional fourth channel was derived from channel 3. Light was taken from both sides of the source S and collimated by lenses L1 and L2. The semi-reflecting plate SR1 divided the left-hand beam. Three

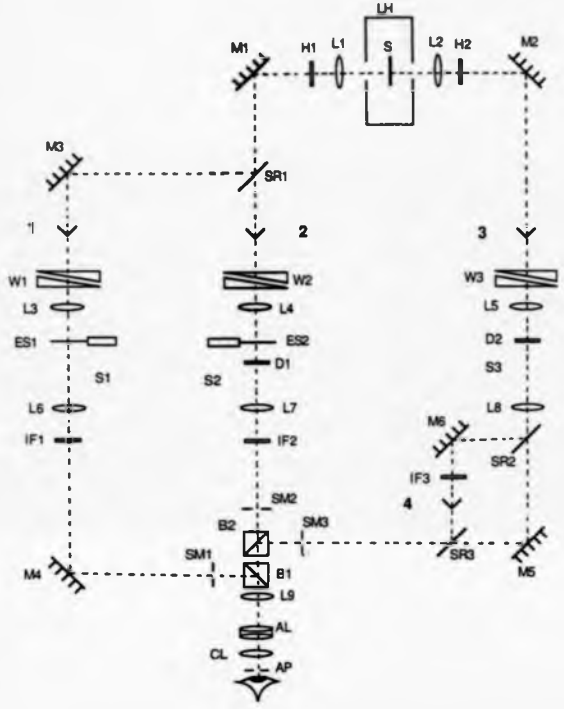


Figure 2.1 The Maxwellian-view system.

individual light channels were thus derived from the source. The beams were interrupted by compensated neutral density wedges, W1, W2, and W3. Lenses L3, L4, and L5 brought the beams to intermediate foci at the stops S1, S2, and S3; the shutters which controlled the time course of channels 1 and 2 were situated at the stops. The light beams were then recollimated by lenses L6, L7, and L8. The beam in the optional fourth channel was derived from that in channel 3 by means of the semi-reflector SR2, and then the two were recombined at SR3. The spectral contents of channels 1, 2, and 4 were controlled by interference filters IF1, IF2, and IF3. The spatial configurations of the beams were controlled by stimulus masks SM1, SM2, and SM3. The three beams were combined by biprisms B1 and B2, and brought by lens L9 to a common focus at the artificial pupil AP. All lenses were achromatic doublets, and all mirrors were front-silvered. A detailed description of the system now follows.

The light source S was a single 24-V, 150-W tungsten-iodide lamp with a compact filament (Atlas, A1/216). It was powered by a regulated DC power supply with ramped switch-on and switch-off designed to prolong lamp life. The lamp was mounted within a lamp house LH which reduced scattered light. Light emerged through apertures on each side of the lamp house to be collimated by lenses L1 and L2, resulting in two parallel beams of light. Heat-reflecting filters H1 and H2 (Balzers, Calflex) attenuated unwanted long-wavelength radiation. The left hand beam was split by the half-silvered semi-reflecting plate SR1. Thus three individual light channels were derived. The level of light output from the source was continously monitored by a silicon photodiode placed in channel 2.

The channels were interrupted by rectangular compensated neutral density wedges, W1, W2, and W3, the positions of which were controlled by pulse-driven DC motors and monitored with high-linearity potentiometers.

Lenses L3, L4, and L5 formed intermediate foci at the stops S1, S2, and S3. Electromagnetic shutters ES1 and ES2 interrupted channels 1 and 2 at the stops. Fast switching of a light channel on or off at such a focus requires only a small movement. The light-flash rise and fall times were less than 2 ms between 10% and 90% of maximum.

In order to increase uniformity of the large stimulus fields produced by channels 2 and 3, ground-glass diffusing plates D1 and D2 were placed at the intermediate foci of these channels. These plates removed any discontinuities in luminance across the field which might result from the lamp filament. In effect, the light images at the diffusing plates formed secondary sources.

Light from the secondary sources was recollimated by lenses L6, L7, and L8. The light beam in channel 3 could be split into two by semi-reflecting plate SR2 to produce an optional fourth channel. The intensities of both channels 3 and 4 were varied by means of wedge W3; in addition neutral density filters (NDFs) could be inserted into any channel. Channel 4 was recombined with channel 3 by means of semi-reflector SR3.

The spectral compositions of those channels giving monochromatic light were controlled with Balzers B40 interference filters, IF1, IF2, and IF3. Filters IF1 and IF2 were placed on motor-driven wheels which allowed easy filter changeover during experimental runs.

Light in channel 2 and, after reflection by mirrors M4 and M5, light in channels 1 and 3 transilluminated stimulus masks, SM1, SM2, and SM3, which controlled stimulus size and shape. The small stimulus masks were photographic transparencies (Kodalith film). The masks were mounted on precision X-Y slides to facilitate alignment of the stimulus fields.

Biprisms B1 and B2 combined light from the three channels and lens L9 brought the beams to a focus at the artificial pupil AP. The image at AP was larger than and concentric with the artificial pupil (except when a small stimulus mask was in place). For later experiments the achromatizing lens AL (Bedford and Wyszecki, 1947) was added to the apparatus. The lens CL was a correcting lens appropriate for the subject making the observations.

Position of the subject's head was stabilized by means of a dental bite-bar. This was attached to an X-Y-Z sliding mount which allowed precise alignment of the subject's pupil with that of the apparatus. The artificial pupil was of diameter 2 mm. (Spring and Stiles (1948) found that natural pupil diameter decreased slightly below 2 mm in only 2 out of 12 subjects for luminances values of around 4 to 5 log trolands. Maximum retinal luminance levels in the present study did not exceed 4.5 log trolands.)

2.2.2 Stimuli

All stimulus fields were circular. The test fields were of diameter 1.05 degrees of visual angle. The test flash duration was 200 ms. For measurements of test spectral sensitivity the test flash was produced by channel 2 and for measurements of field spectral sensitivity by channel 1. The main conditioning field, used in measurements of field spectral sensitivity, was produced by channel 2. It subtended 10 degrees. After preliminary measurements in each set of field spectral sensitivity measurements (Section 2.2.4) it was present continuously. The auxiliary field subtended either 1.05 or 10 degrees and was presented continuously in those experiments in which it was used. It was produced by channel 3 alone or by channels 3 and 4 combined (see below). In measurements of test

spectral sensitivity for a colour discrimination criterion a white comparison flash, identical in size, shape, and duration to the monochromatic test flash, was provided by channel 1; it was presented 1 s after the monochromatic test flash.

Spectral compositions of all main fields and those test fields which were monochromatic were controlled by interference filters (Balzers, type B40) with wavelength of peak transmission ranging from 398 nm to 704 nm and with half-height full bandwidths of not more than 14 nm. Those auxiliary fields and test fields which were white consisted of broad band light from channel 3 or channel 1 respectively (correlated colour temperatures are given later). In those experiments in which the auxiliary field was of mixed monochromatic and white light, the spectral distribution of the monochromatic component was controlled by an interference filter, IF3, placed in channel 4.

In some experiments an array of four small red or white fixation spots arranged in a square of side 3 degrees of visual angle was introduced. All stimulus fields used in an experiment, and the fixation array if present, were arranged concentrically in the subject's field of view. Stimuli configurations are shown in the experimental chapters.

2.2.3 Calibrations

Stability of light source. Fig. 2.2 is a graph of the light-output of the lamp over time recorded from the photodiode situated in channel 2. Excursions about the mean did not exceed 0.01 log volts.

Neutral density filters and wedges. Neutral density filters (NDFs) (Wratten) were calibrated for relative transmittance over 300 nm to 800 nm

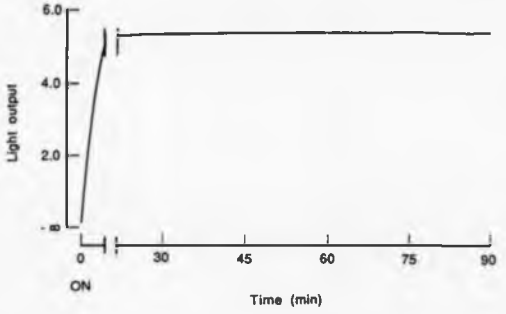


Figure 2.2 Light output of the lamp over time, recorded from the photodiode in channel 2 in volts.

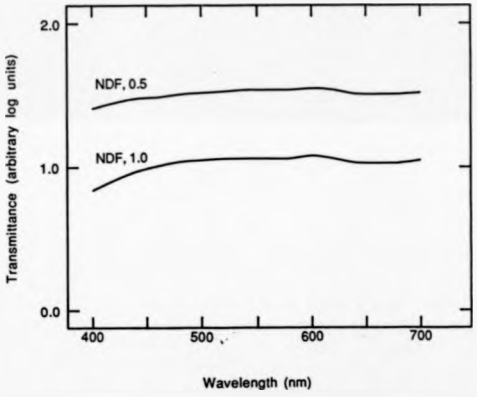


Figure 2.3 Transmittance of two typical NDFs over the visible spectrum. The numbers indicate nominal density

with a Pye-Unicam SP8-100 scanning spectrophotometer. (The spectrophotometer itself was calibrated for wavelength on each use by plotting the transmission of Holmium Oxide and Didymium samples.) Typical plots are shown in Fig. 2.3; between 400 and 500 nm there is a rise in transmittance of about 0.2 log units for each log unit of density; there is then a rough plateau in relative transmittance from about 500 nm to 700 nm. The actual attenuation produced by each NDF, of the light transmitted by each interference filter, was calibrated in situ with the photodiode system described below. These in-situ measurements were used to calculate the intensity measured or used in experimental observations.

The neutral density wedges were calibrated in situ, again for the light transmitted by each interference filter with which they were used. Plots of log transmittance against position of wedge W2 are shown in Fig. 2.4 for four of the interference filters used.

Interference filters. Each interference filter was calibrated for spectral transmission with the Pye-Unicam spectrophotometer. Typical plots for three of the interference filters are shown in Fig. 2.5. The wavelength of peak transmittance and the half-height full bandwidth were obtained from the spectrophotometer recordings. Half-height full bandwidths were between 6 and 14 nm. For interference filters with peak transmittance wavelengths < 460 nm, leakage at 600 nm was less than -3.0 log units of maximum. To further reduce long-wavelength leakage, by a factor of -4.0 log units, a gelatin blocking filter (Ilford, No 621) was attached to each of those interference filters.

Intensity of monochromatic stimuli. Absolute and relative spectral outputs of each channel were measured (for each tungsten-iodide lamp used) at the artificial pupil of the apparatus. Measurements were made with a

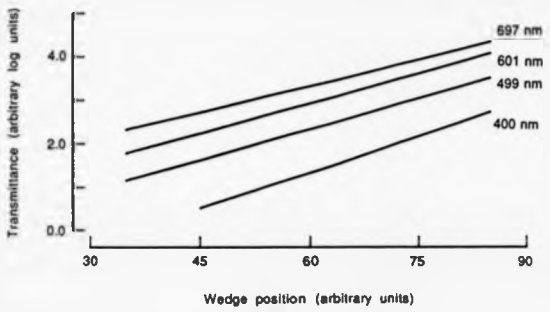


Figure 2.4 Transmittance of the wedge W2 with typical interference filters. The wavelength of maximum transmission of the interference filters is indicated. The curves have been displaced vertically for clarity.

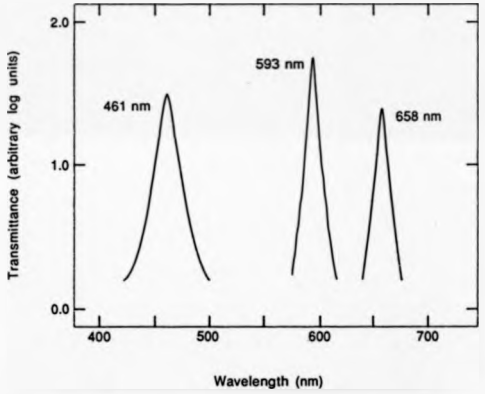


Figure 2.5 Transmittance of typical interference filters over the visible spectrum. Wavelength of maximum transmission is indicated.

low-noise EG&G silicon photodiode (PV-100A), operated in the photovoltaic mode and connected to a linear amplifier and digital multimeter. A non-polarizing Schott glass infra-red-blocking filter (BG21) was mounted in front of the photodiode. Departures from linearity of the photodiode system over a 3-log-unit intensity range (0.005 V to 6.43 V) were less than 0.022 log units.

The photodiode system itself was calibrated against a Hilger-Schwarz vacuum thermopile (FT16) to determine its absolute and relative spectral responsivities. Precautions taken against UV and IR radiation contaminating the calibration included the use of a silica window in the thermopile and a 1-cm-thick water filter placed in front of the thermopile. The thermopile was calibrated by the National Physical Laboratory for both absolute and relative spectral responsivity.

Colour temperature of white stimuli. The colour temperature of the white light from channel 3 was calibrated against a standard source by the following method. A cube of side 2.5 cm, with matt white surfaces, was positioned such that light emerging from the artificial pupil illuminated one face. An adjacent face was illuminated with light from a 100 watt tungsten lamp (with diffusing surface) which had previously been calibrated by a colour temperature meter (Megatron Ltd). Colour conversion filters (Kodak) were inserted into the light beams to produce a visual colour match of the two illuminated faces of the cube. From the results, the colour temperature of the light from channel 3 was calculated to be 3400 K. A bipartite field of white light from channel 1 and from channel 3 was then arranged, and colour conversion filters were inserted into channel 1 until a match for colour temperature was obtained.

Luminance of white stimuli. The luminances required for the auxiliary field, derived from channel 3, were set (again for each tungsten-iodide lamp used) by means of a minimally distinct border (MDB) match (Boynton and Kaiser, 1968; Wagner and Boynton, 1972). A bipartite field of angular subtense 10 deg was composed of white light from channel 3 and monochromatic light of wavelength 562 nm from channel 2; the latter was fixed at an intensity which had been calculated to be equivalent to the retinal illuminance in photopic trolands (Td) required from channel 3. The retinal illuminances used were 300, 1000, 3000, 10,000, and 30,000 Td (2.48 to 4.48 log Td). Six readings were taken of the wedge position in channel 3 at which the border appeared to be minimal. A bracketing procedure was used (settings were made alternately from above or below the match intensity). The mean wedge value was used in experiments.

This method was checked by means of a heterochromatic brightness matching technique which employed a photometrically calibrated incandescent lamp kindly provided to Dr David Foster by Dr Brian Crawford. This lamp was positioned near the artificial pupil and a brightness match between light from the lamp and light from channel 3 was made by varying the intensity of the lamp. A bracketing procedure was used and six readings were taken. The mean intensity of the lamp was read from the calibrations in log photopic trolands.

Stimulus masks. The diameter of each small photographic mask was measured with a travelling microscope. The diameter of the stimulus fields resulting from these masks was calculated to be 1.05($\pm$0.01) deg of visual angle subtended at the eye.

2.2.4 Procedure

General. Preliminary tests of subjects' visual acuity (Snellen and Near Vision) and colour vision were carried out for each eye separately. All subjects had normal or corrected-to-normal acuity. Colour vision was assessed with the Farnsworth-Munsell 100 Hue arrangement test (100 Hue test) (Farnsworth, 1957; Fletcher and Voke, 1985), the City University Test (TCU test) (Fletcher and Voke, 1985), and a Rayleigh match using a Pickford-Nicolson anomaloscope (Pickford and Lakowski, 1960).

All experiments were carried out monocularly with the right eye and all measurements were made foveally. At the start of each set of observations general checks and any necessary rearrangements of the apparatus were made. Any channel not required was blocked. The alignment of each remaining light beam with respect to the artificial pupil was checked, and mirrors M4 and M5 (Fig. 2.1) were adjusted such that the artificial pupil was symmetrically filled with light. The stimulus masks required for the experiment were inserted; the subject adjusted first the bite-bar mount and second the mask X-Y slides, such that the stimulus fields and fixation array if present appeared concentric with respect to each other and to the artificial pupil. Stimulus-flash time-course was checked with a photodiode and an oscilloscope.

The subject dark adapted for ten minutes and then started making threshold measurements. Test-flash presentation was controlled by the subject with a push-button box. The test flash could not be presented more often than once every 2 s to prevent habituation. The intensity of either the test or main stimulus field was controlled by the subject using the push-button box which altered the position of the selected wedge. The subject thus had no non-visual feedback relating to wedge position.

All threshold settings were made using variations of the method of adjustment, as described below. The test-flash wavelength was varied in ascending then descending order (or vice versa) to offset carry-over and sequence effects. Three threshold settings were made at each wavelength; thus six values were obtained, or 12 if the double sequence was repeated, and the mean taken to give a datum point. To ensure that the subject was adapted to the experimental conditions, a sequence of three threshold settings was recorded only when the range of these settings was less than about 0.1 log units.

Test spectral sensitivity measurements. To obtain a test spectral sensitivity function, the wavelength of the flash being detected was varied and threshold intensity of the test field was measured at each wavelength. Measurements were made in the presence of an auxiliary field of diameter either 10^{o} or 1.05^{o}. Each threshold setting was obtained in the following manner. First, the subject set the intensity of the test flash such that the test flash was at criterion level. Next, the intensity was reduced so that the test flash was imperceptible. Finally, the intensity was increased slowly until the test flash was just at criterion level; this intensity was recorded. In most measurements of TSS the criterion was for simple detection. In some measurements (described in Chapter 3) the criterion was for colour discrimination.

Field spectral sensitivity measurements. In these measurements, the wavelength of the main field was varied and the log reciprocal intensity of the main field which raised test flash threshold by 0.3 log unit was measured. This method of direct field adjustment is discussed in the Introduction (Section 1.3.2). In preliminary measurements the subject made four threshold settings of the test flash (by the method described above) with zero main field; these measurements were either of absolute threshold

or of increment threshold on an auxiliary field of diameter 1.05^{o}. Intensity of the test field was then set 0.3 log units above its mean threshold. The main field was introduced, and its intensity set, so that the test flash was returned to threshold, in the following way. First, the intensity of the main field was set at a level at which the test flash was perceptible. Next, the intensity of the main field was increased so that the test flash was imperceptible. Finally, the main-field intensity was decreased slowly until the test flash was just perceptible; this intensity was recorded.

2.2.5 Subjects

Four subjects with normal colour vision participated in experiments using the Maxwellian-view system. Relevant details are as follows:

SG Male, experienced in psychophysical observations, unaware of purpose of experiments, age 22 yr, right eye Snellen acuity 6/4.

MOS Male, experienced in psychophysical observations, unaware of purpose of experiments, age 22 yr, corrected right eye Snellen acuity 6/5.

DHF Male, experienced in psychophysical observations, aware of purpose of experiments, age 39 yr, corrected right eye Snellen acuity 6/4

RSS Female, author, experienced in psychophysical observations, age 27 yr, corrected right eye Snellen acuity 6/5.

Details of other subjects are given in the relevant experimental chapters.

2.3 Clinical measurements: special purpose visual perimeter

2.3.1 Apparatus

The visual perimeter employed for experiments assessing visual function in patients with MS, or ON, or both, was redesigned for certain experiments. The two designs are referred to as Perimeter 1 and Perimeter 2.

In all experiments the screen S was a square of aluminium (side, 71 cm). Over its surface were a number of metal sockets, by means of which the test stimuli (derivation explained below) were presented on the background field. For all experiments a chair of adjustable height was used such that the subject's eyes were on the same level as the central socket of the screen S. The subject's head was supported in a firm adjustable headrest, and the screen was viewed through an eyepiece. Either eye could be occluded, and all observations were carried out monocularly.

Perimeter 1. For the experiments described in Section 8.2 the screen S, with a matt-white finish, was uniformly illuminated by the light source which consisted of four tungsten lamps (Bell Reflector, 240-250 V, 100 W) run from by a stabilized DC power supply, positioned such that two lamps, one above and one below the level of the subject's eyes, stood 2 m apart on a line 0.25 m behind the subject.

The test stimuli were derived from LEDs. Two LEDs were used; one was 'red' (Monsanto MV5752) and the other was 'green' (Monsanto MV5252). The luminance of the stimuli produced by the LEDs was controlled by a variable power supply. A potentiometer gauge indicated the current supplied to each LED and thus, after calibrations (see below) indicated the luminance of the

test field. The light from the two LEDs was combined and mixed by means of a fibre optic 'Y' guide. The end of this was inserted into one of the sockets on the screen S. The time courses of the stimuli were controlled electronically by signal generators (Farnell and Wavetek); both red and green LEDs emitted a train of light pulses. These were presented to the subject in one of two ways: either in-phase to give light pulses, consisting of light from both LEDs, alternating with dark pulses; or in antiphase to give light pulses from the red LED alternating with light pulses from the green LED. The temporal profile of the in-phase and antiphase flicker trains were as shown in Fig. 2.6.

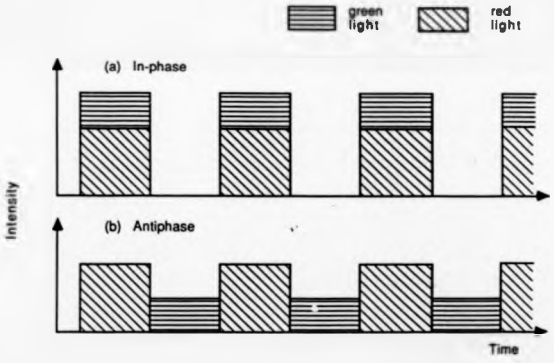


Figure 2.6 Temporal configuration for (a) the in-phase (achromatic) flicker train and (b) the antiphase (chromatic) flicker train.

Perimeter 2. For the experiments described in Sections 7.2, 7.3, and 8.3 the screen S, with a matt-black finish, was viewed through the system shown schematically in Fig. 2.7. The light source LS1 consisted of 9 tungsten bulbs (240 V, 60 W), powered by a stabilized DC power supply, arranged in 3 rows of 3 in the lamp house LH1. The diffusing plate D1 produced uniformity in the light which was then reflected towards the subject, by means of SR (a glass plate which acted as a semi-reflector) through the circular aperture A.

An optional light source LS2 (Fig. 2.7) was added to provide auxiliary fields for the experiments described in Sections 7.2 and 7.3. A tungsten lamp (240 V, 100 W) with diffusing surface, powered from the mains supply, was situated inside a lamp house LH2 which reduced stray light. The light emerged through an aperture above the lamp and illuminated a stimulus mask SM which restricted the size of the beam. A diffusing plate D2, attached to the mask, increased uniformity of the stimulus fields. The light was reflected towards the subject by the beamsplitter BS. A NDF (Wratten) was inserted above the stimulus mask in order to obtain the required auxiliary-field luminance.

Light source LS3 provided the test stimuli for experiments described in Sections 7.2, 7.3, and 8.3. LS3 was a tungsten iodide lamp with a compact filament (24 V, 150 W, Atlas, A1/216). It was run from a regulated DC power supply with ramped switch-on designed to prolong lamp life. The lamp was mounted within the lamp house LH3 which reduced stray light. The light passed through a heat reflecting filter H (Balzers, Calflex) before being focussed onto the ends of the two fibre optic light guides. Two light channels were thus produced. The fibre optic light guides terminated at gaps G1 and G2. At the gaps the light beams could be modified in various ways, thus. A gelatin filter GF1 or GF2 ('Cinemoid' colour

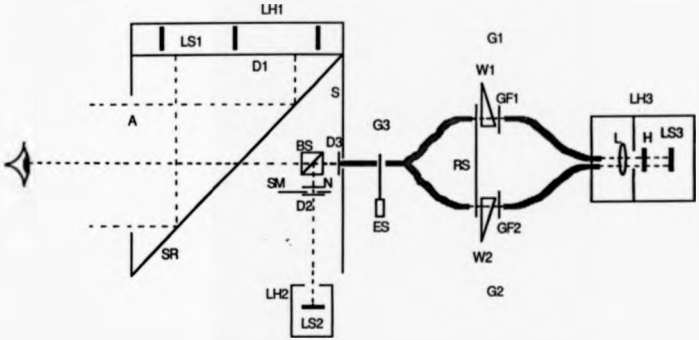


Figure 2.7 Special purpose visual perimeter, Perimeter 2.

Fibre-optic cable

filters, Strand Electronic & Engineering Company Ltd) could be inserted into either gap. A 'green' and a 'red' filter were used. Rotary neutral density wedges W1 and W2 interrupted the beams at the gaps G1 and G2. Each wedge was moved through the light beam by hand. NDFs (Wratten) could be introduced to further adjust the luminance of the stimulus field.

A shutter RS, rotated by a stepping motor controlled by a signal generator (Wavetek), interrupted the beams at gaps G1 and G2. This rotating shutter had transparent and dark sectors of equal size, thus producing a square-wave train of light and dark pulses of equal duration. (RS could be stationary, with one channel open for single test flashes.) When both channels were open the phase of the two flicker trains relative to each other could be changed by moving G1, along the plane of the shutter, relative to G2. In particular the two types of flicker train described above for the LED system could be produced: in-phase and antiphase. The temporal profiles of the in-phase and antiphase flicker trains were as shown in Fig. 2.6.

After the gaps G1 and G2 the two light beams were combined and mixed by means of a fibre optic 'Y' guide. At gap G3 an electromagnetic shutter ES interrupted the light beam. It could be used to open the channel for 3 s or 200 ms, with rise and fall times of 2 ms between 10% and 90% of maximum. Finally a last section of fibre optic guide terminated in a socket at the screen S. A diffusing plate D3 was inserted over the socket to increase uniformity of the stimulus field.

2.3.2 Stimuli

The stimulus configuration and parameters are given in Chapters 7 and 8, in which the experiments carried out using the visual perimeters are

described.

2.3.3 Calibrations

Background fields. These were calibrated for colour temperature with the colour temperature meter, and for luminance with a SEI photometer (Salford Electronic Instruments Ltd, in turn calibrated against the Maxwellian-view system described in Section 2.2). The values for these parameters are given in the descriptions of individual experiments.

Auxiliary field. This was used in the experiments described in Chapter 7. The NDF N (Fig. 2.7), which has the same characteristics as those NDFs described in Section 2.2.3, was present for all experiments in which the auxiliary field was used and also for the calibrations. The colour temperature of the auxiliary field, measured with the colour temperature meter, was 3400 K. The luminance, calibrated with the SEI photometer, was 2.2 log $cd.m^{-2}$.

Spectral content of test fields derived from Perimeter 1. The wavelength of maximum brightness of each LED was determined in the following way. The light from the LED was passed through a monochromator (Applied Photophysics Ltd, M300) and an observer set the wavelength scale such that the transmitted light was at maximum brightness. Four observers each made eight settings, and the mean was taken. The maximum-emission wavelength was 630 nm for the red LED and 530 nm for the green LED. The full wavelength scale was scanned and no visible side bands were found for either LED. The monochromator itself was calibrated against the Maxwellian-view system for relative and absolute spectral properties.

Luminance of test fields derived from Perimeter 1. LED light output for current input, as monitored with a high-linearity potentiometer, was calibrated with the EG&G photodiode system described in Section 2.2.3. In the experiments the green LED was set to give a luminance of 1.78 log $cd.m^{-2}$ to which the luminance of the red LED was matched, as described in Section 8.2.1.

Time course of test fields derived from Perimeter 1. The frequencies of the flicker trains were measured with a storage oscilloscope and the frequency selector of the signal generator was found to be accurate within a tolerance of 1%. The duration of the flicker train was preset to 3 s.

Spectral content of test fields derived from Perimeter 2. The spectral emission of each channel with the gelatin filter in place was calibrated radiometrically with the monochromator and the EG&G photodiode system. The channel not being calibrated was blocked. Measurements were made at approximately 5 nm intervals. The plots of light output measured in relative log units against wavelength for the red gelatin in channel 1 and the green gelatin in channel 2 are shown in Fig. 2.8. With the red gelatin filter in place, channel 1 gave maximum emission at 640 nm with half-height cut-on wavelength of 607 nm. Channel 2 with the green gelatin filter in place gave maximum emission at 540 nm with half-height full bandwidth of 62 nm.

The colour temperature of the white test field was calibrated in the following manner. The colour temperature of the background field, on which the test fields were superimposed in the experimental situation, was used as a standard. A section of the background field was blocked so that the test field was surrounded by the background field and not superimposed on it. Next, colour correcting filters (Wratten) were inserted into the

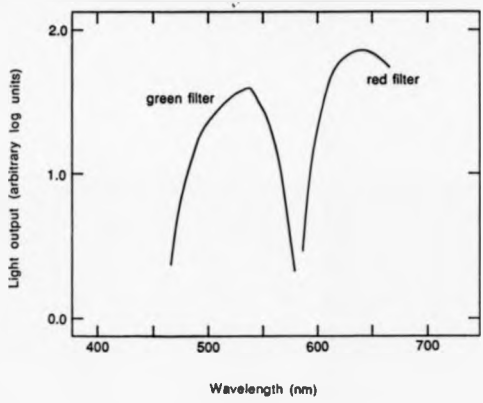


Figure 2.8 Light output, over the visible spectrum, of the fibre optic system for the red gelatine filter in channel 1, and for the green gelatine filter in channel 2.

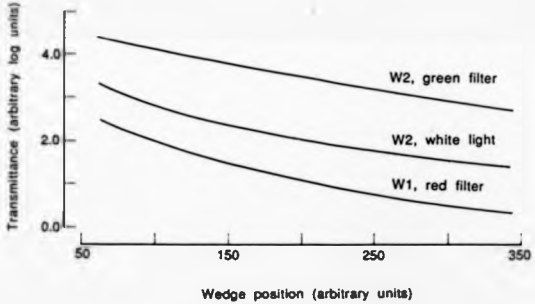


Figure 2.9 Transmittance of the wedges, W1 and W2, for the filter conditions indicated ('white light' was with no gelatine filter). The curves have been displaced vertically for clarity.

system until the test field matched the background field for colour temperature. The unfiltered test field was calculated to have a colour temperature of 3400 K.

Luminance of test fields derived from Perimeter 2. The luminance was controlled by neutral density wedges, W1 and W2, and a NDF which could be inserted at G2. The neutral density wedges were calibrated, in situ for each spectral distribution with which they were used, either radiometrically or photometrically as described below. The plots of wedge transmittance against wedge position are shown in Fig. 2.9 for W2 with the green bandpass gelatin filter, W2 with white light, and W1 with the red long-pass gelatin filter.

The data for W2 with the green gelatin filter were obtained from a radiometric calibration with the EG&G photodiode system as this filter had a relatively small bandwidth. For the white light and the long-pass red gelatin filter it was necessary to use photometric calibrations. For W2 with white light, the auxiliary field (derived from source LS2, Fig. 2.7; calibrations above) was used as the standard. The auxiliary field was presented adjacent to the white test field from channel 2, and a heterochromatic brightness match was made by adjusting the position of the wedge W2. A bracketing procedure was used; two observers each made eight matches and the mean of these were taken. This procedure was repeated for a range of auxiliary-field luminance, produced by inserting NDFs (density calibrated with the SEI photometer) above the stimulus mask SM (Fig. 2.7), until points over the whole wedge had been calibrated.

The calibration of the wedge W1 for red light was carried out by means of heterochromatic flicker matches. The standard was the white light from channel 2. The apparatus was set to give antiphase flicker (see Section

2.3.1) consisting of red light pulses from channel 1 alternating with white light pulses from channel 2. The position of one wedge was fixed and a bracketing technique was used to obtain eight settings, from each of two observers, of the other wedge at which the flicker was minimal. This procedure was repeated until points over the whole of wedge W1 had been calibrated.

The NDF used in channel 2 had similar transmittance properties to those NDFs described in Section 2.2.3. This filter was used to vary the luminance of white stimulus fields only. Its density for white light with respect to the human eye was calibrated with the SEI photometer with the auxiliary field as light source.

In the experiments described in Chapter 7, a range of preselected wedge positions was used and the luminances of the resulting stimuli were derived from the relevant graph. For those experiments in which the stimulus was a flicker train (Section 8.3), the luminance of the red component was set at 2.12 log cd.m^{-2} and the luminance of the green component was matched to that.

Time course of test fields derived from Perimeter 2. The electromagnetic shutter ES (Fig. 2.7) was preset to produce stimuli of duration either 3 s for the flickering stimuli or 200 ms for the flash stimuli. The frequencies of the flicker trains was calibrated as described above and found to be accurate within a tolerance of 1%.

2.3.4 Procedure

Preliminary tests of visual acuity and colour vision (using the TCU test) were carried out for each eye separately. All observations were made

monocularly; the retinal site tested is given in Chapters 7 and 8.

Before each observation session began, the subject was settled into position in a fully adjustable chair as follows. The head rest of the chair was adjusted until the subject was comfortable. The height of the chair was then adjusted such that the subject's eyes were at the same height as the central socket of the screen S. The eyepiece was moved into place and the eye not under test was lightly occluded.

The subject was instructed on the fixation procedure (described in Chapters 7 and 8) and was then given demonstrations of the extremes of the test stimuli which were to be used. For example if critical flicker frequency (CFF) was to be measured, then stimuli flickering at alternately low and high frequencies were shown until the subject felt confident about making a decision. Some subjects required more demonstrations than others. Next the subject was informed of the procedure to be followed in each trial. Thus, on a cue from the experimenter the subject was to fixate the fixation target, and then to press the button that initiated stimulus onset, after which the gaze was to be directed away from the fixation target (to prevent local adaptation occurring), and a response was to be given "yes" or "no".

For those experiments in Section 8.2 the method of limits (Engen, 1971) was used to measure thresholds. Because order effects can influence results obtained with the method of limits, for the experiments described in Sections 7.2, 7.3, and 8.3 the method of constant stimuli was used; the stimuli were presented according to a randomized block design which minimized order and carry-over effects. Further details are given in the relevant experimental chapters.

2.3.5 Subjects

Patients of Dr J.R. Heron, Consultant Neurologist, North Staffordshire Royal Infirmary, took part in the experiments. The patients were classified according to the criteria of McDonald and Halliday (1977) by Dr Heron and either Dr R.E. Jones or Dr W. Honan, Registrars. Details are given in the relevant experimental chapters. A normal control was matched to each patient for age ($\pm$ 5 yr) and sex.

Chapter 3

Test spectral sensitivity curves obtained on white auxiliary fields

3 Test spectral sensitivity curves obtained on white auxiliary fields

3.1 Introduction

The TSS curve obtained in the presence of a large white field was probably first demonstrated by Stiles and Crawford (1933), as described in Section 1.3.3. The curves they obtained, using a relatively large test flash of constant duration with a large white surround, are shown in Fig. 1.10. The peaks in the foveal curves occurred in the short-wavelength (S) region of the spectrum at around 440 nm, in the medium-wavelength (M) region at 538 nm, and in the long-wavelength (L) region at 602 nm (means over two subjects).

Later, Sperling and his colleagues showed similar curves produced both by human subjects and by rhesus monkeys (eg Sidley and Sperling, 1967; Sperling et al., 1968; Sperling and Harwerth, 1971). More recently, other workers (King-Smith, 1975; King-Smith and Carden, 1976; Verriest and Uvijls, 1977; Harwerth and Levi, 1977; Zrenner, 1977; Zrenner and Kruger, 1981; Kuyk, 1982) have also obtained such curves, all determined under a similar experimental paradigm: simple detection of a relatively large, relatively long test flash presented in the centre of a white background field larger than the test flash and of moderate-to-high intensity. Some of the studies cited above present data obtained from non-human primates. Others have compared normal human data with that from subjects with congenital or acquired deficiencies of the visual system. In this chapter I shall present results from normal human subjects only (but see Chapter 6 for discussion on and experiments with patients with impaired visual function).

The stimulus parameters used in the studies cited above are given in Table 3.1, along with the wavelengths of peak sensitivity obtained in each case for normal human foveal vision. Typically, the peaks in the TSS curve occur at around 440, 530, and 610 nm, the latter often appearing as a shoulder rather than as a true peak. The peaks do not coincide for all studies. This may be a result of the range of parameters used. Also, it should be noted that the choice of test wavelengths, particularly if they are widely spaced through the spectrum, can lead to inaccuracies in estimating the positions of the peaks. For example, Verriest and Uvijls (1977) used only eight wavelengths.

The data shown in Table 3.1 are all for foveal vision; any data in the same studies for extrafoveal vision have been excluded. Three peaks in the TSS curve have been shown for stimulus eccentricities of 1.5^{o} by Harwerth and Levi (1977), 5^{o} by Stiles and Crawford (1933), and 6^{o} by Verriest and Uvijls (1977). For the more peripheral retina, however, it seemed that the L and M peaks were much less prominent (Wooten et al., 1975; Verriest and Uvijls, 1977). Instead, a broad maximum was generally found with peak sensitivity at around 550 nm and it was assumed that the peripheral retina was colour deficient. Kuyk (1982), in fact, found that the three peaks in the TSS could be obtained in the periphery if the test field was made sufficiently large (eg 4.2 to 5.5 deg of visual angle for 45^{o} eccentricity). In the present experiments, measurements were made for foveal vision only.

STUDY	TEST FIELD		AUXILIARY FIELD			SPECTRAL POSITIONS OF PEAKS		
	Size[1] deg	Duration ms	Size[2] deg	Luminance[3] Td	Colour temp. K	S	M nanometres	L
Stiles & Crawford (1933)	0.7x0.16[a]	constant	30-1.28[b]	10140	2800	440	538	602
Sidley & Sperling (1967)	2	100	20	1500	2854	430-450	530	590-610
King-Smith and Carden (1976)	1	200	4	1000	3200	440	530	600
Verriest and Uvijls (1977)	1.9	500	*	10cd.m^{-2} [c]	CIE illum. A	451	553	600
Harwerth and Levi (1977)	1	50	14	9000[d]	equal energy	440	535	610
Zrenner (1977)	10	400	15	30000	5500	450	525	610
Zrenner and Kruger (1981)	4	400	11	5000	5500	440	530	610
Kuyk (1982)	1	250	6.7	1000	5000	450	540	600

Table 3.1 Studies, cited in the text, in which the paradigm of a test flash superimposed on a larger white background or auxiliary field was used in measurements of TSS. Studies on normal human foveal vision only are included. The stimulus parameters, and the wavelength of maximum sensitivity in the region of the three peaks are given.

[1,2] Diameter in degrees of visual angle subtended at the eye, except for:

[a] in which the field was a rectangle; [b] in which the field was an annulus.

[3] Retinal illuminance in Td produced by the auxiliary field, except for

[c] where luminance of the field was given in cd.m^{-2}.

[d] Lower values were also used.

* Value not given.

3.1.1 Explanations of the three-peaked TSS curve

Sperling and Harwerth (1971) and King-Smith and Carden (1976) have argued that the TSS curve can not be fitted by the upper envelope of the Stiles π mechanisms: the π_1 curve fits well, the π_4 curve not so well, and the π_5 curve not at all. Sperling and Harwerth (1971) used subtractive-interactive modelling to explain the peaks at 530 and 610 nm. King-Smith and Carden (1976) suggested that such an explanation could be generalized in terms of opponent-colour theories (described in Section 1.3.3). As explained in Chapter 1, the opponent-colour system is thought to be more sensitive to large stimuli and to stimuli of long duration than the luminance system is. Additionally, King-Smith and Carden (1976) and King-Smith and Kranda (1981) suggested that white backgrounds of moderate to high intensities act to depress the sensitivity of the luminance system relative to that of the opponent-colour system; that is, the white field causes achromatic adaptation of the luminance system.

With this explanation in mind, the wavelengths at which the peaks occur in the L and M regions of the spectrum are possible candidates for the wavelengths of peak sensitivity of the red-green opponent channel action spectrum. Thus these wavelengths (530 and 610 nm) are the same as those reported by Werner and Wooten (1979) for extrema in the average chromatic valences of the red-green opponent channel. (See also Hurvich and Jameson, 1957.) Further, as described in Section 1.3.3, when the field spectral sensitivity (FSS) curves of the Stiles π mechanisms are determined using a paradigm which would tend to favour the opponent-colour system the resulting curves peak at around the same wavelengths (530 and 610 nm). Thus Foster (1979, 1980, 1981) using a monochromatic auxiliary field spatially coincident with the test field obtained individual L and M FSS curves, which were much sharper than the corresponding Stiles mechanisms π_5

and π_4, and which had peak sensitivities at 610 nm and 530 nm respectively; the paradigm is thought to cause spatial desensitization of the luminance system (Foster, 1981). Finkelstein and Hood (1981, 1982) showed single FSS curves, which had peak sensitivity at 600 nm and 540 nm with a dip at 580 nm, measured using a flashing main field, whose onset was temporally coincident with that of the test flash; it seems likely that this paradigm would cause temporal desensitization of the luminance system.

A summary of the arguments of King-Smith and Carden (1976) is that any particular test flash is detected by that system which is most sensitive under the particular conditions of test-flash size, duration and wavelength, and the background-field intensity and spectral composition. The results of Foster (1981) and Finkelstein and Hood (1981, 1982) show that the list can be extended to include spatial and temporal distributions of the background-field in relation to those of the test flash. In the case of TSS curves obtained for a test flash of diameter 1 deg and duration 200 ms presented on a large white background, King-Smith and Carden (1976) proposed that the large white background causes achromatic desensitization of the luminance system relative to the opponent-colour system. Detection of the test flash is therefore mediated over most of the spectrum by the opponent-colour system, but in the region of 580 nm the luminance system is more sensitive. The evidence to support this claim is as follows.

Firstly, the TSS curve obtained for a colour-detection criterion was very similar to the curve obtained for a simple-detection criterion except in the region around 580 nm, where the trough is deeper for colour discrimination: that is, with the parameters described above a subject will not be able to identify the colour of a test flash of 580 nm light at threshold. Light of wavelengths greater than 600 nm or less than 560 nm, however, will generally be seen as 'coloured' at threshold when presented

on a large white background. By definition, one would expect the colour of a test flash to be apparent at the threshold of the opponent-colour system.

Second, King-Smith and Carden (1976) also obtained TSS curves with a test flash that was small or brief or both. These paradigms would tend to favour the luminance system, and in the resulting curves the M and L peaks were replaced by a single broad peak with maximum sensitivity around 550 nm. (The S peak is lowered more or less, relative to this broad peak, depending on the particular combination of these parameters, but does not appear to change in shape.) Presumably, for the original parameters, the sensitivity of the luminance system is partially reduced by the white background relative to that of the opponent-colour system. Because of the relative shapes of the action spectra it is only at around 580 nm that the luminance system is the more sensitive and thus acts to 'fill in' the trough of the opponent-colour system.

3.1.2 Combination of spatial and achromatic desensitization

In the experiments described below a combination of two paradigms which have been shown to reduce sensitivity of the luminance system, relative to that of the opponent-colour system, was used in measures of TSS. Thus a large white background (King-Smith and Carden, 1976) which was spatially coincident with the test field (Foster, 1981) was used. This combination would cause both achromatic and spatial desensitization of the luminance system, and it was expected that greater isolation of the opponent-colour system would result. In particular, it was anticipated that the trough found for colour-detection thresholds at around 580 nm by King-Smith and Carden (1976) would be revealed by simple-detection thresholds. The background fields are here called auxiliary fields after Foster (1981).

The TSS function was measured in the presence of either an auxiliary field spatially coincident with the test field (the small auxiliary field) or a large white field (the large auxiliary field). The latter paradigm was a replication of that used in the studies cited above, and acted as a control for the effect of the spatial coincidence of the small auxiliary field. In Experiment 1 simple-detection thresholds only were measured for auxiliary-field luminance 1000 Td. In Experiment 2 simple-detection and colour-discrimination thresholds were measured for a range of auxiliary-field luminances.

3.2 Experiment 1

3.2.1 Methods

The apparatus used in this experiment was the Maxwellian-view system described in Section 2.2.1. The configuration of the stimuli was as in Fig. 3.1. The stimuli parameters are also given in Fig. 3.1. Thresholds for a simple-detection criterion were obtained by the method of adjustment as described in Section 2.2.4. Three subjects took part in the experiment; these were DHF, RSS, and SG (details in Section 2.2.5).

3.2.2 Results

The TSS functions obtained are shown in Fig. 3.2. Sensitivities in log quanta.s^{-1}.deg^{-2} are plotted against test-flash wavenumber. Data for RSS and SG are displaced downwards by, respectively, 1 and 2 log units. Open symbols represent the data obtained in the presence of the large auxiliary field, whereas filled symbols shows that obtained in the presence of the small auxiliary field. The vertical bars show $\pm$1SEM where this is larger

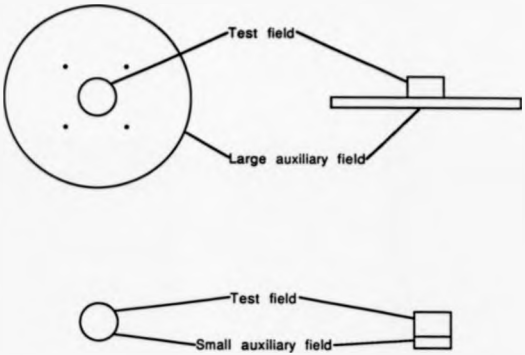


Figure 3.1 The stimulus configuration. The stimuli parameters are given in the table below.

Parameter \ Stimulus Field	Test	Auxiliary
Spectral content	variable	white (3400K)
Diameter (deg)	1.05	1.05 (small) or 10 (large)
Duration (ms)	200	constant
Intensity	variable	1000 Td[1]

[1] Retinal illuminance produced by the auxiliary field.

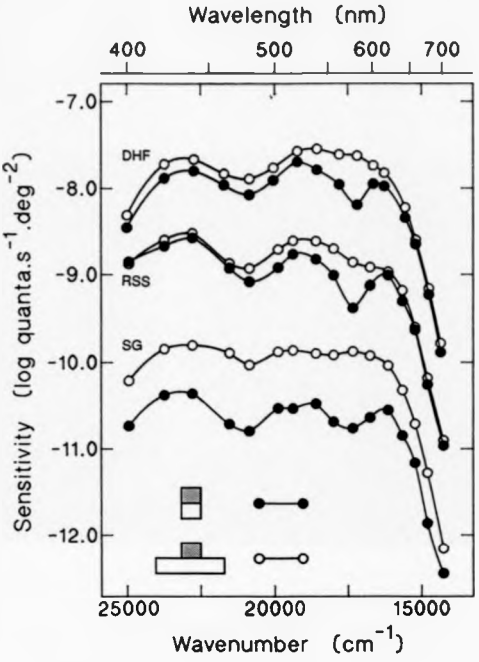


Figure 3.2 Test spectral sensitivity curves obtained on a small white auxiliary field (filled symbols) or a large white auxiliary field (open symbols). (Experiment 1, subjects DHF, RSS, and SG)

than the symbol. Typical SEMs were 0.02 to 0.03 log units. The curves with open symbols in Fig. 3.2 are similar to those obtained in previous studies which used the same paradigm, that is, the large auxiliary field. Peaks occur at around 435, 525 and 580-620 nm, the latter not clearly delineated. The curves with filled symbols in Fig. 3.2, obtained for the auxiliary field spatially coincident with the test field, show one major difference from the upper curves, and that is the trough which occurs at around 580 nm. The trough itself acts to define the M and L peaks much more clearly. The L peak, in particular, appears much sharper than for the curve obtained with the large auxiliary field. Table 3.2 shows, for each subject and each paradigm, the wavelength of maximum sensitivity in the region of each of the three peaks, and the wavelength of minimum sensitivity in the region of each of the two troughs; for the troughs, A refers to that near 480 nm, and B refers to that near 580 nm. The specified wavelength is obtained by Lagrange interpolation and is not the nearest test wavelength used. For the L peak maximum sensitivity occurs at 615 nm for SG and RSS and at 605 nm for DHF. The M peak has maximum sensitivity at 520 nm for DHF, 522 nm for RSS, and at 534 nm for SG, although this peak is not so clear for SG. The M peaks are not so sharp as the L peaks, nor have they been shifted so far along the wavelength axis. An asymmetry between the L and M mechanisms has been reported elsewhere (Stromeyer et al., 1978b; Foster, 1981; Zrenner, 1983; Ronchi, 1983).

Of further interest are the troughs present in the TSS curves. Table 3.3 shows, for each subject, the increase in depth for each trough for the TSS obtained on the small auxiliary field compared with that obtained on the large auxiliary field. For trough B (near 580 nm) this increase was calculated in the following way. The expression $\log N_B - \log N_L$, where N is the quantity of light in quanta.s^{-1}.deg^{-2}, was evaluated for both the small auxiliary field and the large auxiliary field. The L and B

	Subject		
	SG	DHF	RSS
TSS on large auxiliary field			
Peak			
S	434	433	436
M	515	534	525
L	*	*	*
Trough			
A	480	478	478
B	*	*	*
TSS on small auxiliary field			
Peak			
S	431	436	438
M	534	520	522
L	615	605	615
Trough			
A	479	480	481
B	574	582	577

Table 3.2 Wavelength, in nm, of maximum sensitivity in the region of each of the three peaks, and of minimum sensitivity in the region of each of the two troughs, for each of the three subjects. * indicates that a region of maximum or minimum sensitivity could not easily be distinguished in the region of the relevant peak or trough.

	Subject		
	SG	DHF	RSS
Trough			
A	0.23	0.04	0.09
B	0.34	0.37	0.47

Table 3.3 Increased depth of trough, in log quanta.sec^{-1}.deg^{-2}, produced by the small auxiliary field for each subject. For details of calculation see text.

wavelengths used for these calculations were those from the Lagrange interpolation of the data obtained with the small auxiliary field. The result obtained for the large auxiliary field was subtracted from that for the small auxiliary field to give a measure of the increase in depth of the trough caused by making the auxiliary field spatially coincident with the test field. This trough is from 0.34 to 0.47 log units deeper when the small auxiliary field is used (Table 3.3). For trough A (near 480 nm) the calculation was made using the expression $\log N_A - \log N_S$. For one subject, SG, the S peak also seems slightly sharper in the lower curve than in the upper, with a corresponding increase in depth of trough A of 0.23 log units. For RSS the increase is less than 0.1 log units and for DHF it is negligible.

3.2.3 Discussion

Reducing the size of the white auxiliary field such that it is spatially coincident with the test field has had the effect of improving isolation of the opponent-colour system. The luminance system has been subjected both to spatial desensitization (by the edge of the auxiliary field) and to achromatic adaptation (by the white auxiliary field). The activity of the opponent-colour system is now revealed in the region from 520 to 620 nm. Thus the peaks in this region of the spectrum are much sharper than are the corresponding peaks obtained with the large auxiliary field. This sharpening of the peaks is accompanied by the deepening of the trough at around 580 nm, by at least 0.35 log units (Table 3.3). This trough is generally thought to be characteristic of the opponent-colour system. The isolation of the opponent-colour system may still not be complete (see below), but it is much improved.

Other studies have been carried out with the aim of measuring the sensitivity of the opponent-colour system at threshold. Thus, the paradigm of the small auxiliary field, developed by Foster (1979) for measurements of field spectral sensitivity was also used by Krastel et al. (1983, 1984) in measurements of test spectral sensitivity. In addition, these authors showed that a three-peaked TSS curve, with a deep trough at about 580 nm, could be obtained in the peripheral retina if the test and auxiliary fields were large (eg 16 deg of visual angle at 33^{0} eccentricity).

Some approaches to the isolation of the opponent-colour system have employed test stimuli with modified spatial and temporal profiles that eliminate the spatial and temporal transients at the stimulus edges. The "low-frequency" test stimulus of Thornton and Pugh (1983a,b) had bell-shaped spatial and temporal distributions which were designed so that the Fourier spectra had most energy concentrated at low frequencies. The test spectral sensitivity curves obtained with this low-frequency test stimulus presented on a large white auxiliary field (Thornton and Pugh, 1983a) were similar to those in Fig. 3.2 for the small auxiliary field (filled circles).

If the extent and periodicity of the stimulus are increased the relative power at low frequencies may be still further enhanced. Thus Mullen (1987) used monochromatic sinusoidal gratings superimposed on a large white auxiliary field; for spatial frequencies of below 1 deg^{-1} and a temporal frequency of 0.8 Hz the spectral sensitivity curves obtained for contrast sensitivity were also similar to the curves in Fig. 3.2 for the small auxiliary field (filled circles). The Weber function and the spatial response function for a grating of 577 nm, however, indicated that the opponent-colour system did not contribute to detection at 577 nm, even though sensitivity of the luminance system was depressed in that region.

3.3 Experiment 2

The TSS curves obtained for simple detection of a test flash on an auxiliary field spatially coincident with the test field (curves with solid symbols in Fig. 3.2) are similar to the curves obtained by King-Smith and Carden (1976) for recognition of the colour of a test flash on an auxiliary field larger than the test flash. In particular, a trough is present at around 580 nm in the curves for both paradigms, whereas it is almost absent for simple detection of a test flash on a large auxiliary field (curves with open symbols in Fig. 3.2). Subjects did, in fact, report that in this region of the spectrum the colour of the test flash was often apparent at threshold on the small auxiliary field but not on the large auxiliary field. To investigate these reports, thresholds for both simple-detection and colour-detection criteria were measured at wavelengths spanning the trough at around 580 nm. Instead of absolute judgements of stimulus colour in the colour-detection measurements, a reference white was introduced and the test stimulus judged against that. Formally, therefore, the task was one of colour discrimination. A range of luminance levels of the auxiliary field was tested in these measurements to determine whether there was a limiting effect in the depression of the sensitivity of the luminance system relative to the opponent-colour system. Sperling *et al*. (1967) and Harwerth and Levi (1977) showed that the dip at around 580 nm obtained for a simple-detection criterion with a large white auxiliary field deepened with increasing luminance of that field, reaching a maximum in depth for luminances of 10,000 Td or 3000 Td respectively. It seemed plausible that increasing the luminance of the small auxiliary field would also decrease sensitivity of the luminance system, offering the possibility that the trough at around 580 nm obtained for simple detection would eventually converge on the trough obtained for colour discrimination.

3.3.1 Methods

Threshold measurements were carried out on the small auxiliary field for, separately, a simple-detection and a colour-discrimination criterion by the method of adjustment described in Section 2.2.4. The apparatus used was the Maxwellian-view system. The stimulus configuration and parameters were as shown in Fig. 3.1, except for two details. First, a comparison flash (Section 2.2.2) was added which had colour temperature 3400 K and spatial and temporal profiles identical to those of the test flash; it was presented 1 s after the test flash. Second, luminances of the auxiliary field of 300, 1000, 3000, 10,000, and 30,000 Td were used. One subject, RSS, carried out these measurements.

3.3.2 Results

Results are shown in Fig. 3.3. Sensitivities in log quanta.s^{-1}.deg^{-2} are plotted against test-flash wavenumber. Filled symbols indicate data for simple detection and open symbols for colour discrimination. The vertical bars show $\pm$1SEM where sufficiently large. The pairs of curves (each pair displaced successively downwards by 0.5 log unit) are for increasing luminance of the small auxiliary field as indicated. For simple detection the trough at about 580 nm became progressively deeper with increasing auxiliary-field luminance. The trough for colour discrimination, however, remained substantially the same over auxiliary-field luminances of 300 to 10,000 Td. At 30,000 Td the relative sensitivity for colour discrimination at short and long wavelengths was different from that at lower luminances.

To quantify these changes in trough depth, the difference between mean sensitivity over 577 and 582 nm and over the regions 520 to 566 and 593 to

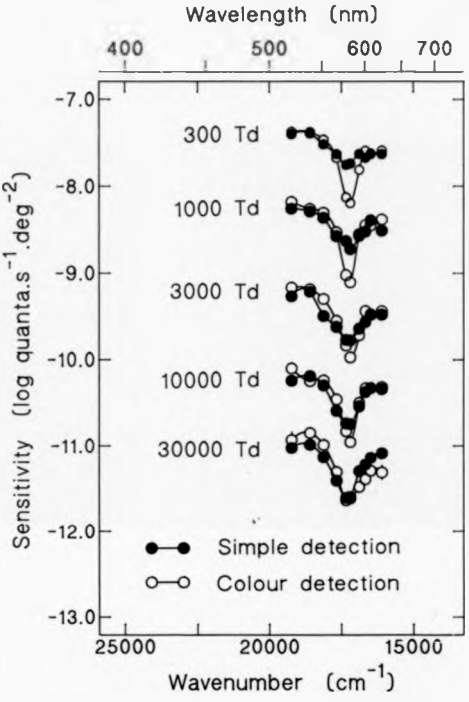


Figure 3.3 Test spectral sensitivity curves obtained for simple-detection (filled symbols) and colour-discrimination (open symbols) criteria on a small white auxiliary field. (Experiment 2, subject RSS)

623 nm was calculated for simple detection and for colour discrimination at each auxiliary-field luminance from 300 to 30,000 Td. For simple detection, there was an increase in trough depth relative to that at 300 Td at each successive luminance level: values were +0.06, +0.12, +0.19, and +0.26 log unit as luminance increased from 1000 Td (see Fig. 3.4a, filled symbols). For colour discrimination, the differences in trough depth relative to that at 300 Td were essentially constant: values were +0.07, -0.10, -0.02, and -0.17 log unit (where there was a change in curve shape) as luminance increased from 1000 Td (see Fig. 3.4a, open symbols). The difference between trough depths for simple detection and colour discrimination decreased with increase in auxiliary-field luminance: values were +0.42, +0.43, +0.19, +0.20, and -0.01 log unit as luminance increased from 300 to 30,000 Td (a positive value indicating a less deep trough for simple detection). These values are plotted in Fig. 3.4b.

The simple-detection data and colour-discrimination data are replotted in the form of threshold-versus-intensity (tvi) curves in Fig. 3.5a and Fig. 3.5b respectively; threshold at each wavelength is plotted against auxiliary-field luminance. The differential effects of auxiliary-field luminance are less evident than in the plot of test spectral sensitivity (Fig. 3.3).

3.3.3 Discussion

Consider first the data for the 30,000 Td auxiliary field. Isolation of the opponent-colour system seemed to be complete. The relative heights, however, of the M and L peaks for colour discrimination on the 30,000 Td auxiliary field were different from those at 10,000 Td and lower. RSS did, in fact, note that the 'white' comparison flash appeared pinkish when presented on the 30,000 Td field. Of relevance here is an investigation by

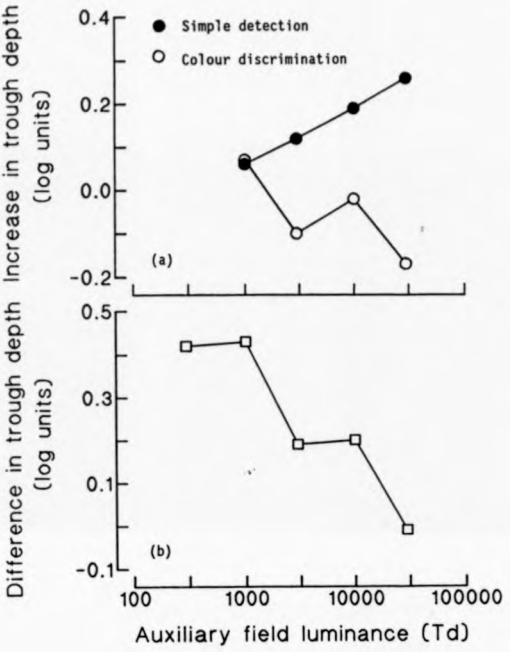


Figure 3.4 (a) Increase in trough depth relative to that at 300 Td for each successive luminance level. Data derived from those shown in Fig. 3.3. For further details see text.

(b) Difference between trough depths for simple detection and colour discrimination. A positive value indicates a less deep trough for simple detection. Data derived from those shown in Fig. 3.3.

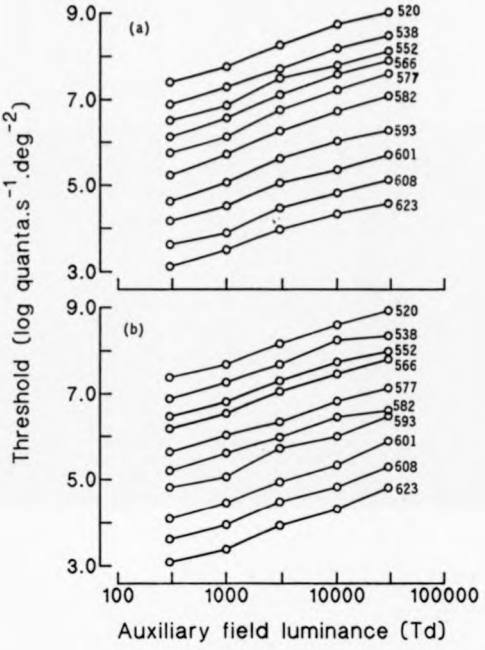


Figure 3.5 Threshold for each wavelength (indicated in the figures) is plotted against luminance of the auxiliary field. The curves have been shifted vertically for clarity.

(a) Simple-detection data. (b) Colour-discrimination data.

Wyszecki (1978) into colour matching at high luminance levels. At luminances of 10,000 Td the relative proportions of M and L primaries required to match the reference white deviated from those at lower luminances.

Consider next data for auxiliary-field luminances of 300 to 10,000 Td. The trough in spectral sensitivity for the simple-detection criterion deepened with increasing auxiliary-field luminance and reached its lowest relative value at auxiliary-field luminances of 3000 and 10,000 Td, where the curves were close to those obtained for colour discrimination. A small residual difference (of the order of 0.2 log unit) between simple-detection and colour-discrimination thresholds was evident at wavelengths close to 580 nm. In contrast, for colour discrimination, the trough in spectral sensitivity remained fairly stable over auxiliary-field luminances of 300 to 10,000 Td. The similarity of detection and discrimination troughs at auxiliary-field luminances of 3000 and 10,000 Td provides strong support for the hypothesis that the small auxiliary field secured isolation of the opponent-colour system at threshold.

Chapter 4

Field spectral sensitivity curves obtained on small white auxiliary fields

4 Field spectral sensitivity curves obtained on small white auxiliary fields

4.1 Introduction

The last chapter described the improved isolation of the red-green opponent-colour pathways in measures of TSS produced by making the white auxiliary field spatially coincident with the test field. The rationale for that paradigm arose partly from evidence that desensitization of the luminance system can be achieved both by a white background field (King-Smith and Carden, 1976) and spatial coincidence of test and auxiliary fields (Foster, 1981). Foster used monochromatic small auxiliary fields in measures of FSS, and obtained spectrally sharpened curves which he explained in terms of desensitization of the luminance, non-opponent system and thus detection by L-M and M-L opponent-colour pathways (see Section 1.3.3). For the present research, it was hypothesized that use of a small white auxiliary field in measures of FSS would further desensitize the non-opponent system, and hence lead to greater isolation of the opponent-colour system in measures of adaptational sensitivity (FSS) as it had in the direct measures of sensitivity (TSS).

4.2 Methods

The apparatus used in this experiment was the Maxwellian-view system described in Section 2.2. Threshold measurements were carried out by the method described in Section 2.2.4. The stimuli configuration was as in Fig. 4.1. Stimuli parameters are also given in Fig. 4.1. Three subjects, DHF, SG, and RSS (details in Section 2.2.5) took part in the experiment. The wavelength, λ, of the test flash was fixed, for all subjects, at 422 nm

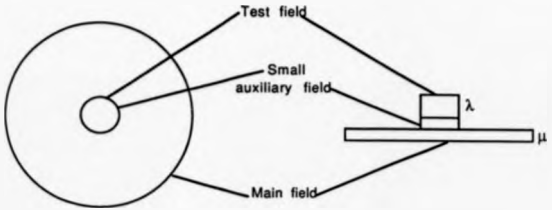


Figure 4.1 The stimulus configuration. The stimuli parameters are given in the table below.

Parameter \ Stimulus Field	Test	Auxiliary	Main
Spectral content	variable	white (3400K)	variable
Diameter (deg)	1.05	1.05	10
Duration (ms)	200	constant	constant
Intensity	0.3 inc.[1]	1000 Td[2]	variable

[1] Test flash intensity was 0.3 log quanta.s^{-1}.deg^{-2} above threshold on the auxiliary field with zero main field.

[2] Retinal illuminance produced by the auxiliary field.

for the S sensitive mechanism and at 608 nm for the L sensitive mechanism; for the M sensitive mechanism it was fixed at 521 nm for subjects SG and RSS and at 531 nm for subject DHF. The choice of these wavelengths was guided by the results of Foster (1981); in particular, for the L sensitive mechanism, spectral sharpening for test flashes of wavelength 610 - 620 nm was at least 0.3 log units greater than for test flashes of wavelength less than 600 nm or greater than 650 nm. Further, pilot studies with the white auxiliary field showed that greater spectral sharpening was obtained with a 608 nm test flash than with a 658 nm test flash. The set of wavelengths, μ, of the main field was taken from the range 401 - 702 nm.

4.3 Results

Figs. 4.2, 4.3, and 4.4 show results for subjects DHF, RSS, and SG respectively. The curves connecting points represented by symbols show field spectral sensitivities for the L (squares), M (circles), and S (diamonds) sensitive mechanisms obtained on the 1.05-deg white auxiliary field. The test-flash wavelength for each field spectral sensitivity curve is indicated. In all cases, sensitivity is expressed as $\log_{10}$ reciprocal threshold in quanta.s^{-1}.deg^{-2}. The vertical bars show ± 1 SEM where this is sufficiently large to be displayed. The curve for the S sensitive mechanism (diamonds) has been displaced downwards by 1.0 log unit for subjects SG and DHF, and by 0.5 log units for subject RSS, in order to show peak sensitivity at approximately the same level for all mechanisms. The rationale for this displacement is discussed in Chapter 5.

4.4 Discussion

The curves for the L and M sensitive mechanisms (shown by the filled squares and circles, respectively, Figs. 4.2 to 4.4) have both changed in

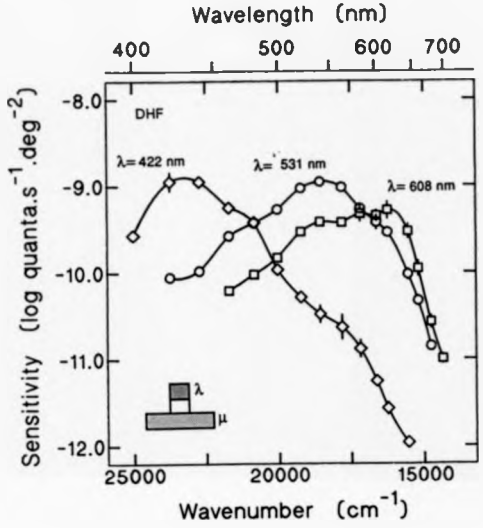


Figure 4.2 Field spectral sensitivity curves, obtained on the small white auxiliary field, for the L (squares), M (circles), and S (diamonds) mechanisms. The test-flash wavelength used for each field curve is indicated. Subject DHF.

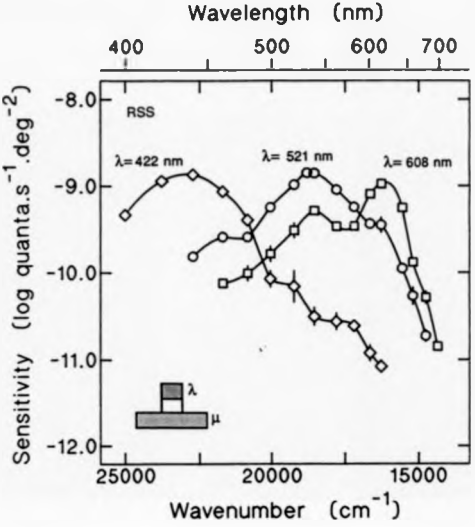


Figure 4.3 Subject RSS. Other details as for Fig. 4.2.

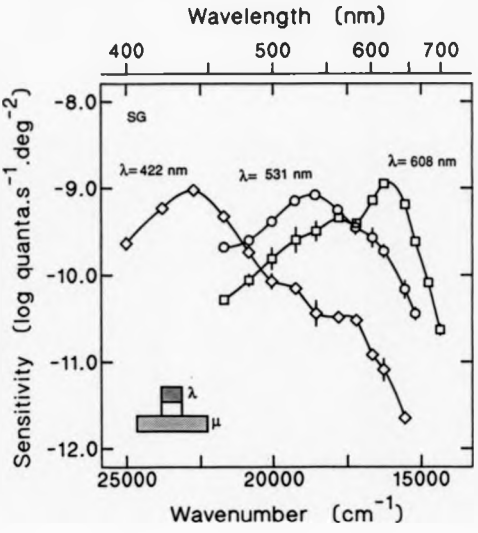


Figure 4.4 Subject SG. Other details as for Fig. 4.2.

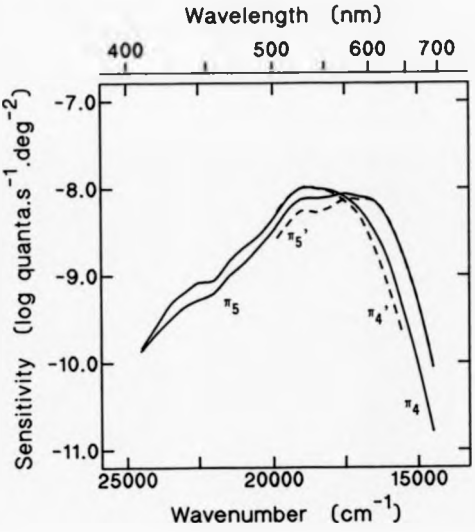


Figure 4.5 Stiles' mechanisms π_4, π_5, π_4', and π_5', plotted from data given in Stiles (1978, p18).

shape relative to the corresponding Stiles mechanisms π_5 and π_4 (plotted in Fig. 4.5). The most obvious change in shape is for the L sensitive mechanism. Stiles' π_5 has a fairly flat top with maximum sensitivity at around 575 nm; here, with the small white auxiliary field, the L sensitive mechanism is narrowed with a sharp peak at around 620 nm. On the short-wavelength side a subsidiary peak is also apparent, the magnitude and position of which varies from subject to subject. For SG and RSS this peak is large enough to define a dip at about 580 nm, reminiscent of that found for the L sensitive mechanism by Finkelstein and Hood (1981). Action spectra obtained from red-sensitive colour-opponent cells in rhesus monkey show similar subsidiary maxima or shoulders on the short-wavelength side (Dow and Gouras, 1973; de Monasterio et al., 1975). Regan (1974) made VEP measurements of the L-sensitive mechanism under conditions which would tend to favour detection by opponent-colour channels; these also have a shoulder on the short-wavelength side. Interestingly, π_5' (plotted in Fig. 4.5) peaks at a longer wavelength than does π_5, and also exhibits a slight shoulder on the short-wavelength side. These similarities of π_5' with the sharpened L-sensitive mechanism shown in Figs. 4.2 to 4.4 are consistent with evidence that for long-wavelength test-threshold increments above 1.2 log units (where Stiles found the π_5' branch in tvi curves) detection is mediated by an opponent mechanism (Wandell and Pugh, 1980).

The effects of the small auxiliary field on the M sensitive mechanism were less pronounced. Such asymmetries in the interaction of L and M signals have been shown previously (evidence cited in Section 3.2.2). The spectrally sharpened M mechanism shows a subsidiary peak or shoulder, complementary to that of the L mechanism, here on the long-wavelength side. There is also evidence, for two subjects, RSS and DHF, of a shoulder on the short-wavelength side of the M mechanism. For the S mechanism there was no apparent sharpening, consistent with research cited in Section 1.3.3 that

signals from the S sensitive cones do not contribute to the luminance system in these detection tasks.

Chapter 5

Unitary opponent-colour processes underlying TSS and FSS?

5 Unitary opponent-colour processes underlying TSS and FSS?

5.1 Introduction

It was suggested in Chapter 3 that the small-white-auxiliary-field paradigm causes desensitization of the luminance system, and therefore allows detection of the test flash to be mediated by the opponent-colour system throughout the spectrum. Sensitivity of the opponent-colour system was revealed both in direct measurements of test spectral sensitivity (Chapter 3) and in adaptational measurements of field spectral sensitivity (Chapter 4). A pertinent question is whether unitary opponent-colour mechanisms or channels, each with a spectral sensitivity that is qualitatively the same, underly both these measurements of spectral sensitivity. If test and field action spectra do reveal the same mechanisms then there should be a correspondence between the shape of the two types of curve over the spectral region where both can be measured (Stiles, 1959). Further, over the whole spectrum the upper envelope of all field action spectra should correspond to the test action spectra, when both measurements are made using the same paradigm. Such a correspondence in the data for the small white auxiliary field is described next.

First, the wavelengths of peak sensitivity for the TSS curve are close to those for the sharpened L, M, and S field curves (see Table 5.1). Second, when the vertical positions of the S field curve was allowed to vary, the upper envelope of the three field curves provided a close fit to the TSS curve. The latter point is demonstrated in Fig. 5.1, a summary graph; data were obtained with the small white auxiliary field, and previously shown in Fig. 3.2 or 4.2 to 4.4. In Fig. 5.1 filled symbols denote TSS data and open symbols denote the upper envelope of FSS data.

	Subject		
	SG	DHF	RSS
Peak in TSS			
S	431	436	438
M	534	520	522
L	615	605	615
Peak in FSS			
S	440	430	436
M	536	543	535
L	621	617	621

Table 5.1 Wavelength, in nm, of maximum sensitivity in the region of each of the three peaks in the TSS curve (from Chapter 3, Experiment 1), and in the region of the peak in each FSS curve (from Chapter 4), for each of the three subjects.

For further details see figure legend. For the purposes of the present work the important point is that the cross-over point between the M and L field curves, represented by the trough near 580 nm of the upper envelope (open symbols, Fig. 5.1), occurs at a similar wavelength to the trough in sensitivity in the TSS curve (filled symbols, Fig. 5.1). This supports the hypothesis that the direct and the adaptational measures of the red-green opponent channel are mediated by unitary mechanisms. That this correspondence is not trivial can be tested by changing the paradigm in such a way that a change in curve shape occurs. The resultant TSS curve should be similar to the upper envelope of the resultant FSS curves. A change in curve shape could be obtained, for example, by altering the spectral content of the auxiliary field. This is the subject of the present experiment.

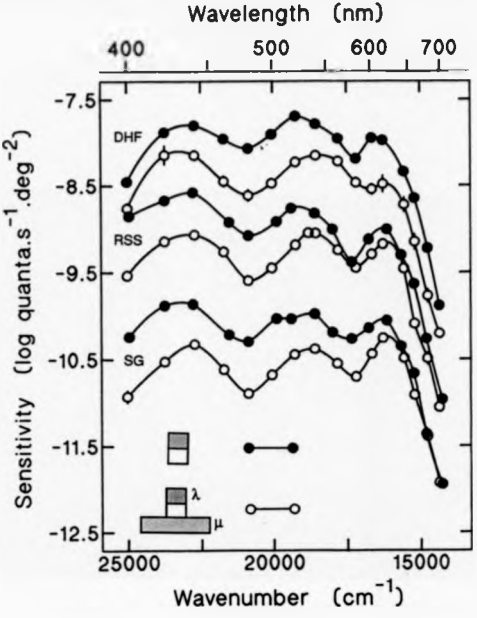


Figure 5.1 Summary graph. All data were obtained with the small white auxiliary field, and previously shown in Fig. 3.2 or 4.2 to 4.4. Filled symbols denote TSS data. Open symbols denote FSS data which was selected to show the upper envelope of the three field curves in the following way. The data for the S-sensitive field action spectra was displaced downwards by 1.0 log unit for SG and DHF and by 0.5 log unit for RSS, thus showing peak sensitivity at approximately the same level as for the M and L curve (see below). Data points forming the upper envelope of the three FSS curves were then selected for plotting, and displaced upwards close to the TSS curve. The fact that the height of the S field curve had to be displaced downwards relative to the M and L curves is compatible with the Weber-Fechner fractions for π mechanisms (Stiles, 1959); that for π_3 was four or five times greater than those for π_4 and π_5.

Data for RSS and SG were displaced downwards by, respectively, 1.0 and 2.0 log units for clarity.

5.2 Methods

Measurements were made, for simple-detection criteria, of TSS, as described in Section 3.2.1, and of FSS for the L- and M-sensitive mechanisms, as described in Section 4.2. The paradigm here differed in that the spectral content of the auxiliary field varied. The auxiliary field was either 'greenish', consisting of monochromatic light of wavelength 497 nm and white light in the proportion 1:2, or 'pink', where the monochromatic light was of wavelength 604 nm. The luminance of the auxiliary field remained at 1000 Td. One subject, RSS, made these measurements.

5.3 Results

The TSS data obtained for the different auxiliary-field spectral contents are shown in Fig. 5.2. The uppermost curve (previously shown in Fig. 3.2) is for the white auxiliary field, the middle curve is for the greenish auxiliary field, and the lowermost curve is for the pink auxiliary field. Both TSS and FSS data obtained for the greenish auxiliary field are shown in Fig. 5.3, for the pink auxiliary field in Fig. 5.4, and, for comparison, data for the white auxiliary field previously shown in Figs. 3.2 and 4.3 are replotted here in Fig. 5.5. Solid symbols denote TSS data, and open circles and squares denote FSS data for, respectively, the M- and L-sensitive mechanisms.

Consider first the TSS data (Fig. 5.2). The effect of the greenish auxiliary field was to depress the M peak relative to the L peak and, thus shift the position of the trough to around 560 nm (from around 580 nm on the white auxiliary field). The pink auxiliary field had the opposite effect, depressing the L peak relative to the M peak and shifting the

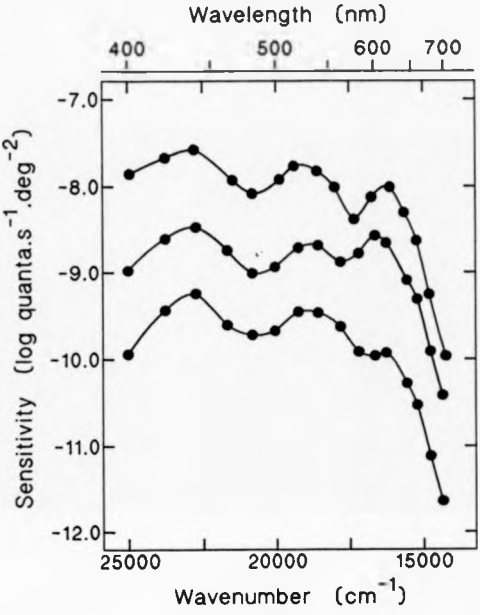


Figure 5.2 Test spectral sensitivities obtained on small auxiliary fields. Uppermost curve: white auxiliary field. Middle curve: greenish auxiliary field. Lowermost curve: pink auxiliary field.

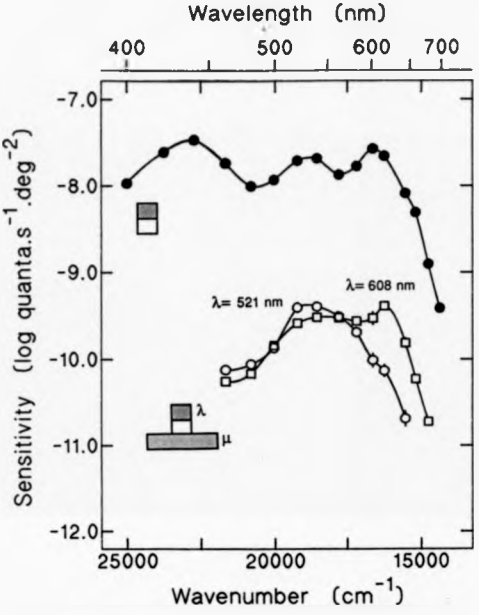


Figure 5.3 Spectral sensitivities obtained on the small greenish auxiliary field. Filled symbols indicate test spectral sensitivity. Open circles and squares indicate field spectral sensitivity data for, respectively, the M- and L-sensitive mechanisms. Subject RSS.

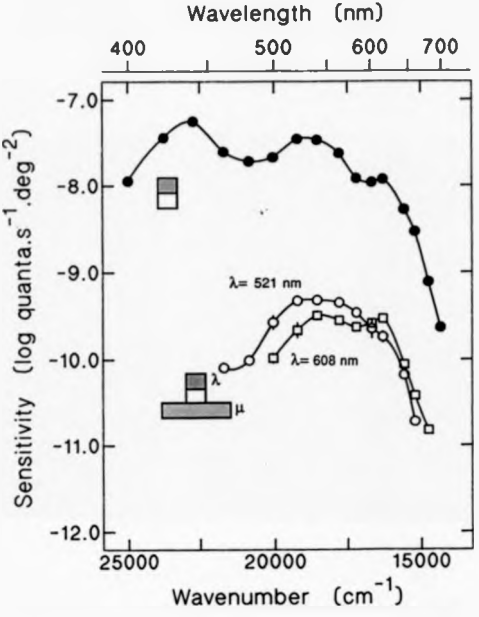


Figure 5.4 Spectral sensitivities obtained on the small pink auxiliary field. Other details as for Fig. 5.3.

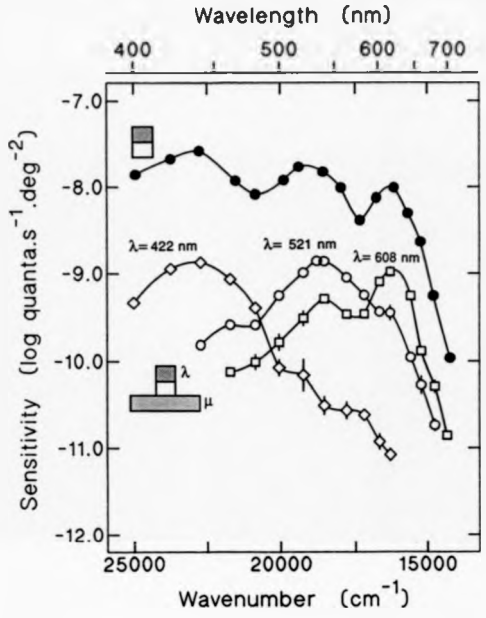


Figure 5.5 Spectral sensitivities obtained on the small white auxiliary field, replotted from Figs. 3.2 and 4.3. Open diamonds indicate field spectral sensitivity for the S-sensitive mechanism. Other details as for Fig. 5.3.

position of the trough to around 600 nm. Consider next the FSS data. The changes in the curves were effectively the same as the change in shape of the TSS curve, as predicted above. Thus the greenish auxiliary field (Fig. 5.3) depressed the M curve relative to the L curve, and the crossover point of the two curves moved to around 560 nm. The pink auxiliary field (Fig. 5.4) depressed the L curve relative to the M curve, and the crossover point moved to around 600 nm.

5.4 Discussion

The data provide support for the notion that opponent-colour mechanisms underlying test and field action spectra act in a unitary fashion. Thus the upper envelopes of the field curves correspond to the test curve when both are measured with the same paradigm. The notch in test sensitivity at around 580 nm for a white auxiliary field presumably corresponds to the equilibrium point in the underlying red-green opponent channel, and this equilibrium point is represented in the field data by the crossover point of the M and L curves. If the equilibrium point is moved along the wavelength scale by means of chromatic adaptation then this is reflected in both test and field data.

A displacement of the trough in measurements of TSS as a result of adaptation to large chromatic auxiliary fields has been shown by Sperling and Harwerth (1971) and Thornton and Pugh (1983b). Further, Mollon and Fach (1987) showed that the wavelength at which the trough occurs in the TSS curve obtained for a large auxiliary field can be predicted by interpolating a tritanopic confusion line on the CIE chromaticity diagram through the point corresponding to the auxiliary field, a finding which supports the view that the trough represents the equilibrium point of the red-green opponent channel.

Chapter 6

Opponent processing in subjects with inherited and acquired deficiencies?

6 Opponent processing in subjects with inherited and acquired deficiencies?

It was suggested in previous chapters that use of a white auxiliary field spatially coincident with the test field improves isolation of the red-green opponent-colour channel in normal subjects. The small-auxiliary-field paradigm may help in understanding the nature of colour deficiencies. Two types of impairment will be considered: first, the inherited deficiencies protanopia and deuteranopia (see Section 1.5.1); and second, MS and ON, conditions which can result in colour deficiencies, including loss in hue-discrimination, in addition to impairment of other visual functions (see Section 1.5.2). The functioning of opponent processes in these conditions is the subject of this chapter.

6.1 Experiment 1: Subjects with protanopia or deuteranopia

Hurvich and Jameson are the modern proponents of the theory that a collapse system underlies dichromacy (described in Section 1.5.1). This theory, although plausible in many respects, is incompatible with the evidence from MSP and molecular genetics cited in Section 1.5.1; that is, it appears that a photopigment is missing in fact and not merely apparently. Further, it seems unnecessary to postulate a specific deficiency in the neural mechanisms underlying the red-green opponent channel to explain deficiencies in opponent processing in dichromats. Consider the deuteranope, who has L photopigment only, and assume that he has a full cone mosaic with L photopigment replacing M photopigment. Assume further that the neural connections are identical to those in the normal subject. Thus signals from 'M' cones oppose those from L cones in the L-M and M-L channels. In the deuteranope, with only L photopigment, the actual input to those channels will be L-L; in the protanope the input

will be M-M. The output for both dichromats, therefore, will be severely abnormal over the spectral range in which the red-green opponent channel normally operates. The L+M channel, which is the major or only contribution to the luminance system in the normal subject, will in the dichromat receive signals in the form M+M or L+L. In dichromats, therefore, the 'L+M' system will be affected only to the degree of the diminished sensitivity over portions of the spectrum. Thus, as Wald (1966) suggested, the protanope has extremely high thresholds in the long-wavelength region where the sensitivity of the M-sensitive mechanism falls well below that of the normal L-sensitive mechanism, and the deuteranope is only slightly deficient in the middle-wave region because in this region the sensitivity of the L-sensitive mechanism is only slightly less than that of the normal M-sensitive mechanism. In both types of dichromat, therefore, the luminance system would be more sensitive than the opponent-colour system probably for any visual condition, and would usually mediate detection at threshold. Further, if neural mechanisms remain the same as in the normal, regardless of the spectral sensitivity of the photopigments, then the dichromat's perception of white is understandable (cf Hurvich and Jameson, 1962).

Dain and King-Smith (1981) provided evidence supporting the view that dichromats have only two cone photopigments with signals from either the L- or the M-sensitive pigment feeding both sides of red-green opponent neurones; for example, their results for deuteranopes can be understood in terms of L-centre, L-surround ganglion cells. In the present experiments dichromats were tested with the paradigm which has been shown (Chapter 3) to isolate more clearly the red-green channel of the opponent-colour system in normal subjects. There is the possibility that this effective paradigm might reveal any residual opponent processing in dichromats; such opponent processing would have very different spectral sensitivity to that of a

normal subject, in addition to a reduction in absolute sensitivity.

6.1.1 Methods

Test spectral sensitivity was measured on the small and large auxiliary fields. The apparatus and procedure were identical to those used with normal subjects (Section 3.2.1). Two subjects with a red-green inherited deficiency took part in the experiment: one protanope, ST, age 23 yr, and one deuteranope, IW, age 25 yr, both with normal acuity. The colour vision of these subjects was classified with the 100-Hue Test and a Rayleigh match.

6.1.2 Results

Test spectral sensitivity curves are shown for the protanope, ST, in Fig. 6.1 and for the deuteranope, IW, in Fig. 6.2. Results for subject SG, typical of normal data (Chapter 3), are also shown in each figure for comparison. The curves for each dichromat have been shifted downwards by 1.5 log units for clarity. The upper curve (filled symbols) of each pair represents the TSS obtained in the presence of the large auxiliary field, whereas the lower curve (open symbols) shows that obtained in the presence of the small auxiliary field. The vertical bars show ± 1 SEM where this is sufficiently large. There are two main differences between the normal data and data for the two dichromats. First, the curves for each dichromat have, as expected, only two peaks in contrast to three in the normal curve. The S peak of both dichromats, at around 440 nm, is similar to that of the normal. The second peak is at around 540-560 nm for the protanope and 560-580 nm for the deuteranope.

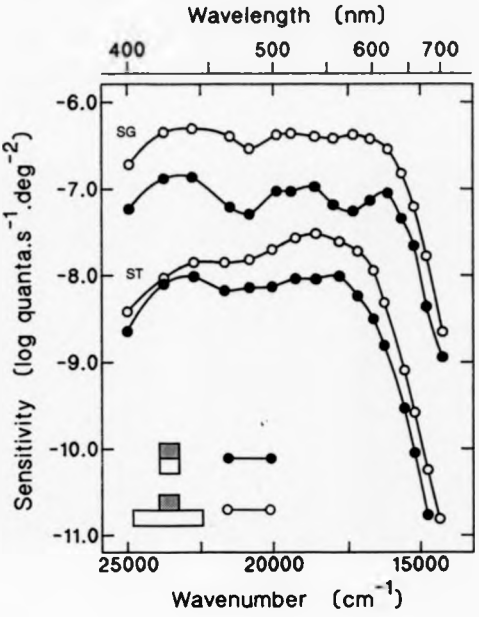


Figure 6.1 Test spectral sensitivity curves obtained on a small white auxiliary field (filled symbols) or a large white auxiliary field (open symbols). Experiment 1. Subjects: SG, normal control; ST, protanope.

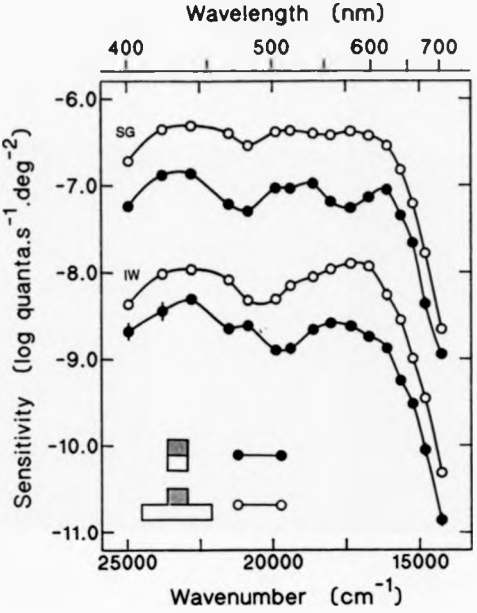


Figure 6.2 Subjects: SG, normal control; IW, deuteranope. Other details as for Fig. 6.1.

The second difference concerns the region for wavelengths longer than 500 nm. For the normal there is a change in shape between the two curves, with a deeper trough at around 580 nm for the small auxiliary field, but there is no difference in relative sensitivity at the L and M peaks compared with that at the S peak. For the dichromats, however, there is no change in shape of the curve above 500 nm, but there is a change in relative sensitivity at the L or M peak compared with that at the S peak. For both dichromats, when the auxiliary-field size is reduced then there is a fall in average sensitivity over 500 to 600 nm if the TSS curves are shifted vertically to match in sensitivity at the S peak; this fall in sensitivity is 0.31 log units for the protanope and 0.32 log units for the deuteranope.

The magnitude of the decrease at each wavelength, produced by making the auxiliary field spatially coincident with the test field, is illustrated in Fig. 6.3a for the protanope and in Fig. 6.3b for the deuteranope; the dotted line demonstrates equivalent data for the control subject, shifted vertically to fit data for each dichromat at short wavelengths. For the normal subject, the major effect of the small auxiliary field (revealed by a relatively large decrease) occurs at around 580 nm with a smaller effect at around 470 nm (compare increased depths of each trough produced by the small auxiliary field for this subject, Table 3.3). Over the remaining wavelengths the decrease in sensitivity is fairly constant. For both dichromats, in contrast, the small auxiliary field produces a small decrease in sensitivity over 400 to 440 nm, and a larger, relatively constant, decrease in sensitivity for wavelengths above 500 nm.

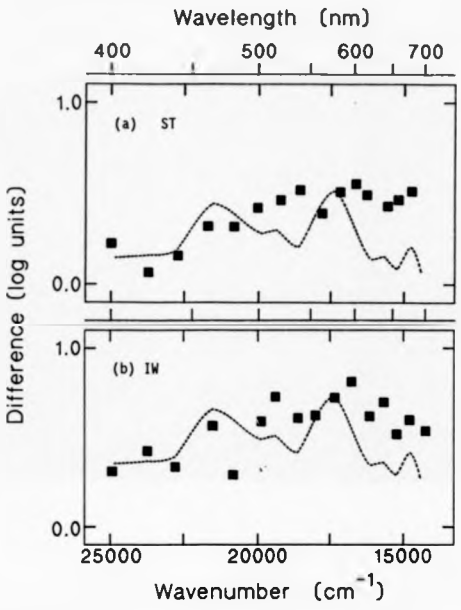


Figure 6.3 (a) Subject ST, protanope. The decrease in sensitivity produced by making the auxiliary field spatially coincident with the test field is plotted against wavelength (symbols). The dotted line shows equivalent data for SG, control subject, shifted vertically to fit the dichromat data at short wavelengths. For further details see text.

(b) Subject IW, deuteranope. Other details as for (a).

6.1.3 Discussion

Test spectral sensitivity curves obtained in the presence of the large auxiliary field for the dichromats are similar to those obtained for a similar paradigm by Verriest and Uvijls (1977). There is no evidence of the trough at 580 nm in the TSS curves for the dichromats on either auxiliary field. As this trough results, in normal subjects, from the opposition of signals from L- and M-sensitive photopigments then it would not be expected for dichromats. The most interesting aspect of the dichromat data is the fall in sensitivity above 500 nm relative to sensitivity at the S peak when the auxiliary field is made spatially coincident with the test field. Such a gross change in relative sensitivity does not occur for normal subjects (compare top curves, normal data, with bottom curves, respectively protanopic and deuteranopic data, in Figs 6.1 and 6.2). There is, however, a fall in sensitivity for normal subjects in the region of the trough at around 580 nm when the small auxiliary field is introduced; the trough is deepened by 0.34 to 0.47 log units (see Table 3.3). This deepening was ascribed in Chapter 3 to the depression of the sensitivity of the luminance system, relative to that of the opponent-colour system, produced by high spatial-frequency masking. The fall in sensitivity for the dichromats of around 0.3 log units over the region 500 to 600 nm relative to the S peak (Fig. 6.3) might reflect a similar effect. That is, the sensitivity of the dichromat's luminance system is depressed by high spatial-frequency masking, as in the normal, but the sensitivity of the opponent-colour system is so severely impaired, as suggested above, that the sensitivity of the luminance system is still, probably by far, the greater. The results do not resolve the issue of the presence or otherwise of a red-green opponent-colour channel in dichromats. They do, however, indicate that the sensitivity of the dichromatic luminance system can be modified in a similar manner to that of normals.

That is, the neural connections of the dichromatic luminance system could be normal, the abnormal shape of the luminance action spectrum resulting because signals arise from only M or only L photopigments.

6.2 Experiment 2: subject with multiple sclerosis and optic neuritis

A review of the literature on which system, luminance or chromatic, was the more affected in patients with MS, or ON, or both was given in Section 1.5.2. In Chapter 7 an investigation of chromatic and luminance function in a number of patients is described. Here, TSS curves for the small and large auxiliary fields were obtained from a single patient with MS and stable ON as an illustration of the use of the small-auxiliary-field paradigm in this context.

6.2.1 Methods

The stimulus parameters and configuration are shown in Fig. 6.4. The large background field was introduced (compare stimuli used for normals and dichromats, Fig. 3.1) to approximate more closely the stimuli used for the clinical study of Chapter 7. The wavelengths used were limited to the region of maximum interest (499 to 678 nm) to avoid tiring the patient.

Subjects. The two subjects who took part in this experiment were RSS, a normal control (details in Section 2.2.5), and CB, a patient (male, 35 yr) with clinically definite MS. CB had had right ON ten and eight years previously. In addition spinal and brain stem lesions had been noted; in all five relapses had occurred. Duration of the disease was 13 years. CB's right eye, tested in the present experiments, had a Snellen acuity of 6/5 and a 100-Hue error score of 140 with no obvious polarity.

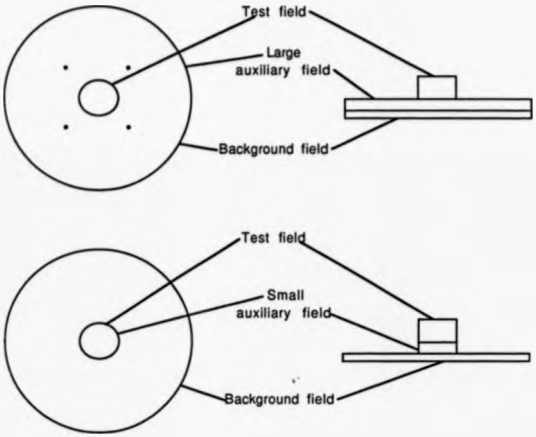


Figure 6.4 The stimulus configuration used in Experiment 2. The stimuli parameters are given in the table below.

Parameter \ Stimulus Field	Test	Auxiliary	Background
Spectral content	variable	white (3400 K)	white (3400 K)
Diameter (deg)	1.05	1.05 (small) or 10 (large)	10
Duration (ms)	200	constant	constant
Intensity	variable	1000 Td [1]	100 Td [1]

[1] Retinal illuminance produced by that field

6.2.2 Results

Test spectral sensitivity functions for both subjects are shown in Fig. 6.5. The data for patient CB have been displaced downwards by 1.0 log unit for clarity. The upper curve (filled symbols) in each pair represents the TSS obtained in the presence of the large auxiliary field, and the lower curve (open symbols) that obtained in the presence of the small auxiliary field. The vertical bars show $\pm$1SEM where this is larger than the symbol.

The data for RSS, obtained here with a large background field, were similar to those for the same subject obtained without such a field (compare Fig. 3.2). For the small auxiliary field, maximum sensitivity was at 520 nm (M peak) and 608 nm (L peak), and minimum sensitivity in the trough region was at 581 nm (compare Table 3.2). The increase in depth of the trough for the small auxiliary field (calculated in the manner described in Section 3.2.2) was 0.32 log units.

Sensitivity for CB, compared to that for RSS, showed an average significant decrease of 0.46 log units ($t = 2.37$, $p < 0.005$) for the small auxiliary field and 0.62 log units ($t = 2.67$, $p < 0.01$) for the large auxiliary field. The shapes of the two curves for this subject were, however, similar to those of the normal. For the small auxiliary field, CB gave maximum sensitivity at 532 nm (M peak) and 612 nm (L peak), and minimum sensitivity in the trough at 582 nm. Further, the increase in depth of the trough for CB was 0.44 log units, within normal limits (see Table 3.3).

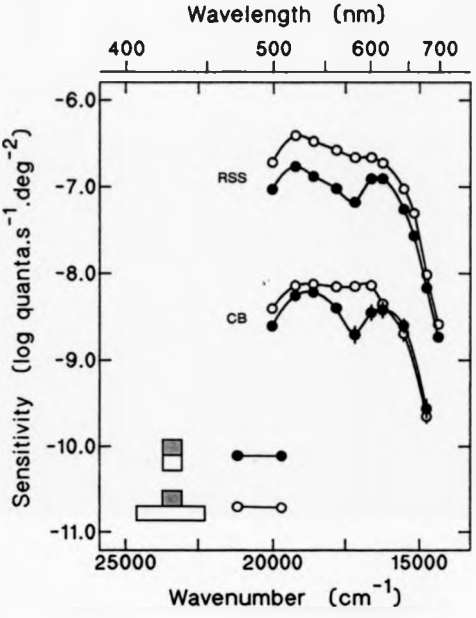


Figure 6.5 Test spectral sensitivity curves obtained on a small white auxiliary field (filled symbols) or a large white auxiliary field (open symbols). Experiment 2. Subjects: RSS, normal control; CB, patient with MS and ON.

6.2.3 Discussion

The results for the patient tested in this experiment do not support claims that, in MS, impairment of chromatic function is greater than that of luminance function; the TSS curve measured in the presence of the small auxiliary field has the deep trough at around 580 nm which is associated with activity of the opponent-colour system (see Section 3.2.3). The average absolute sensitivity, however, was reduced in the patient by about 0.5 log units relative to that for the normal subject. This fact implies a generalized loss in sensitivity for both chromatic and luminance function. The data presented here were for one patient only, and need not, of course, hold for the population as a whole. The effects of MS tend to vary in severity (see Section 1.5.2). In addition, it has been postulated that there are subgroups of patients in which either chromatic or luminance sensitivity is more severely impaired (Alvarez and King-Smith, 1984). The next chapter describes an investigation of chromatic and luminance function in a group of patients with a paradigm modified from the present procedure.

Chapter 7

Clinical application of the small-auxiliary-field paradigm

7 Clinical application of the small-auxiliary-field paradigm

7.1 Introduction

In Chapter 6 test spectral sensitivity curves measured in the presence of a large and of a small auxiliary field were shown for a patient with MS and ON. That patient had normal opponent-colour function, at least for the fovea, although he had depressed sensitivity throughout the spectrum relative to the sensitivity of the normal subject.

There are a number of disadvantages to the investigation of patients by means of observations on the Maxwellian-view system, as explained in Section 2.1. In particular, obtaining full and accurate TSS curves is time-consuming and entails several visits by the patient. Therefore, for the experiments described in this chapter, a special purpose visual perimeter was used and the number of threshold measurements was reduced to four, chosen with the aim of giving maximum information on the relative sensitivities of the luminance and opponent-colour systems. Effectively, two vertical slices through the TSS curves were obtained by measuring thresholds for a red and a white test flash on small and large auxiliary fields. The rationale for choosing these four conditions is given next.

For the normal visual system, a red test flash would be detected by the opponent-colour system even when presented on the large auxiliary field, and, therefore, no improvement in isolation of this system would be expected from measuring threshold for a red test flash on the small auxiliary field. The high spatial-frequency masking caused by the small auxiliary field does, however, produce a small decrease in sensitivity of the opponent-colour system (see Fig. 3.2) of 0.1 or 0.2 log units. For

test-flash wavelengths around 580 nm, the situation would be different. Here the sensitivity of the luminance system on the large auxiliary field would be considerably greater than that of the opponent-colour system, whereas for the small auxiliary field the difference in sensitivity of the two systems would be small. The combination of desensitization of the opponent-colour system and the luminance system by high spatial-frequency masking gives about a 0.4 log unit increase in trough depth on the small auxiliary field relative to that on the large auxiliary field (see Table 3.3).

Thus for two wavelengths, of 610 nm (or longer) and 580 nm, subtracting the decrease in sensitivity for the red test flash, obtained by reducing the size of the auxiliary field, from that for the yellow is equivalent to the procedure for calculating the increased depth of trough from full TSS curves, (described in Section 3.2.2).

Consider now these measurements in comparing chromatic and luminance function in patients. If the two systems were equally affected in a particular patient, then the TSS curves would simply be lower than those for a normal, the relative sensitivities at the two wavelengths on the two auxiliary fields remaining the same as for a normal. This was the case for patient CB (see Fig. 6.4). If for a particular patient, the relative sensitivities differ from normal then a selective impairment of either the opponent-colour or the luminance system is indicated.

In fact, there is no need to use a chromatic test flash (wavelength 580 nm) to measure the decrease in sensitivity of the luminance system; a white test flash should be equally efficient. To confirm this assumption, the following pilot study was carried out.

The Maxwellian-view system was used to present either a white or a yellow (582 nm) test flash (diameter 1 deg, duration 200 ms) superimposed on either the small or the large auxiliary field (3000 Td). Subjects DHF and MOS (details in Section 2.2.5) made simple-detection threshold measurements for each condition by the method described in Section 2.2.4. The results in log Td (±SEM) are shown in Table 7.1.

	White Test Flash		Yellow Test Flash	
	Large Aux.	Small Aux.	Large Aux.	Small Aux.
Subject				
DHF	2.055(0.039)	2.505(0.026)	2.083(0.019)	2.511(0.023)
MOS	1.774(0.015)	2.315(0.068)	1.782(0.053)	2.317(0.069)

Table 7.1. Threshold in log Td. For explanation see text.

For each subject and for each auxiliary field there was no significant difference between thresholds for the white and yellow test flashes ($t \leq 0.17$, $df = 10$, $p >> 0.05$). There was a highly significant difference, however, for each subject and each test flash between thresholds on different auxiliary field sizes ($t \geq 6.15$, df 10 , $p < 0.005$).

A control experiment was necessary to assess the effectiveness of the paradigm in revealing a selective impairment in the processing of chromatic or luminance information. This control experiment was carried out on a subject with inherited sex-linked dichromacy; no evidence of opponency for middle to long wavelengths is observed in such subjects with a similar paradigm to that used here (Section 6.1).

7.2 Control experiment

7.2.1 Methods

The stimuli for these experiments were presented by means of Perimeter 2 (Section 2.3.1). The stimulus configuration and parameters are shown in Fig. 7.1. The data were collected by the randomized block method described in Section 2.3.4. The parameter varied was the intensity of the test field, with a step interval of approximately 0.1 log unit. The criterion used was simple detection of the test flash. The subjects were ST (protanope, details in Section 6.1.2) and SG (normal subject, details in Section 2.2.5).

Data Analysis. Raw data were analyzed by computer-based probit analysis (Finney, 1952). This gave the 50% detection point corresponding to stimulus threshold, and a standard deviation which may be interpreted as the variability associated with that threshold (Patterson et al.,1980).

7.2.2 Results

Thresholds for ST (protanope) and SG (normal) are plotted in Fig. 7.2. Data for ST have been displaced vertically upwards by 0.5 log unit for clarity. As would be expected, the thresholds for white light, within a particular auxiliary field, are similar for the two subjects. The threshold for red light, however, is much higher for the protanope than for the normal subject by about 0.9 log unit on the large auxiliary field (see Verriest and Uvijls, 1977, who also measured thresholds on a large auxiliary field for protanopes and normals). On the small auxiliary field the protanope's threshold for the red test flash is raised still further, by about 1.6 log unit above normal.

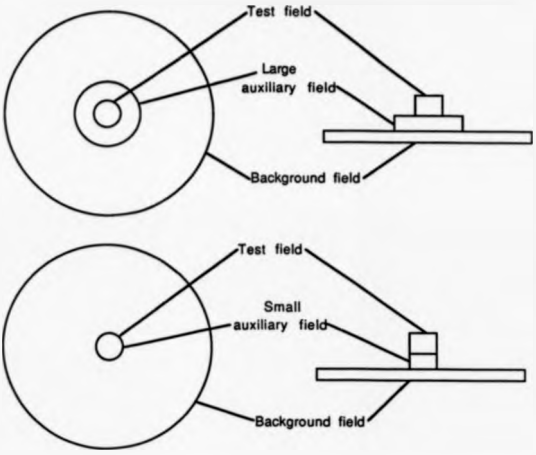


Figure 7.1 The stimulus configuration. The stimuli parameters are given in the table below.

Parameter \ Stimulus Field	Test	Auxiliary	Background
Spectral content	white (4000 K) or red[1]	white (3400 K)	white (2600 K)
Diameter (deg)	0.25	0.25 (small) or 1.25 (large)	24
Duration	200	constant	constant
Luminance ($cd.m^{-2}$)	variable	160	35

[1] Controlled by a red gelatine filter; in situ, maximum emission was 640 nm and half-height cut-on wavelength was 607 nm.

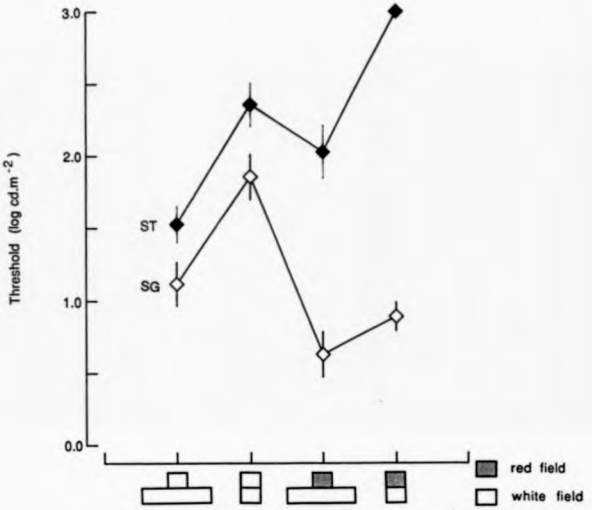


Figure 7.2 Threshold in log cd.m^{-2} for the white and red test flashes on the small and large auxiliary fields. Control experiment. Subjects: SG, normal control; ST, protanope.

The decrease in sensitivity to the white test flash caused by reducing the size of the auxiliary field is 0.83 log unit for the protanope, similar to that for the normal subject (0.74 log unit). For the red test flash, however, the equivalent decrease is of greater magnitude for the protanope (about 0.9 log unit) than for the normal subject (0.26 log unit). Moreover, for the red test flash the decrease for the protanope is slightly larger than that for the white test flash, whereas for the normal subject the decrease is much smaller for the red test flash than for the white.

7.2.3 Discussion

Consider first the results for SG which are typical of normal subjects (see below). Sensitivity for the white test flash is reduced by 0.74 log units when the auxiliary field is made spatially coincident with the test field; the equivalent reduction for the red test flash is 0.26 log units. Such a disparity for the two test flashes was expected to result from the greater vulnerability of the normal luminance system to the high spatial-frequency masking produced by the small auxiliary field.

Consider now the results for the protanope, ST. First, the paradigm clearly reveals reduced long-wavelength sensitivity (Fig. 7.2). ST's thresholds for white light were within the normal range (see below), yet his thresholds for red light were well outside. Second, the paradigm is sensitive to the loss, or severe spectral modification of, red-green opponent-colour pathways. The depression in sensitivity to the white test flash caused by the high spatial-frequency masking of the small auxiliary field is similar to that for the red test flash (0.83 and approximately 0.9 log units, respectively).

This control experiment suggests that the small-auxiliary-field paradigm offers a sensitive and specific approach to the investigation of opponent-colour and luminance function in patients with MS, or ON, or both.

7.3 Main experiment

7.3.1 Methods

The experimental conditions were as described in Section 7.2.1. The subjects who took part in this experiment were nine patients and nine normal controls. The control subjects were age- and sex-matched to the patients. There were six females and three males in each group. Patients were classified according to the criteria of McDonald and Halliday (1977); details are given in Table 7.2. No patient had nystagmus and none reported difficulty in fixating. All patients had had one or more episodes of ON, but at the time of this investigation none showed active ON and none had central scotomata. No patient had worse Snellen acuity than 6/9, except for patient 7 for whom it was 6/12. For the TCU test, patient 2 gave five tritan errors and patient 3 three tritan errors; patients 5, 6, and 7 could not perform the test. Normal controls all had normal colour vision and Snellen acuity of 6/9 or better.

Data analysis. Raw data were analysed as described in Section 7.2.1. For each condition the mean was then calculated for the normal group and for the patient group.

Patient	Age	Sex	Symptoms	Duration of Disease (yrs)	Classification
1	51	F	Spinal ON	6	Clinically Definite MS
2	31	M	Spinal ON	9	Clinically Definite MS
3	41	M	ON	5	ON
4	48	M	ON	0.5	ON
5	38	F	ON	6	ON
6	26	F	Spinal ON	0.7	Early Probable
7	46	F	ON	3	ON
8	34	F	Spinal ON	10	Clinically Definite
9	44	F	Spinal ON	8	Clinically Definite

Table 7.2 Summary of clinical data for patients who took part in the main experiment.

7.3.2 Results

The mean results for the patients and for the matched normal controls are plotted in Fig. 7.3. For each condition the mean threshold for the patient group was significantly higher ($t \geq 2.75$, $df = 16$, $p < 0.01$), by about 0.4 log unit, than that for the normal group. The mean increases in threshold were numerically very similar; there was a range of only 0.08 log units.

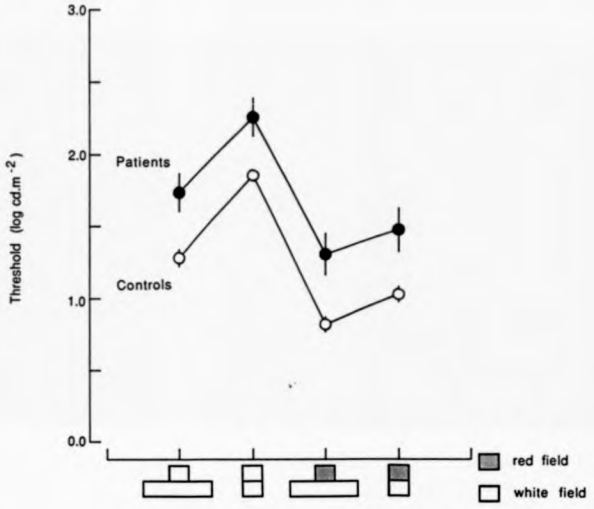


Figure 7.3 Mean thresholds in log cd.m^{-2} for the white and red test flashes on the small and large auxiliary fields. Main experiment. Solid symbols show data for the patient group, and open symbols show data for the normal group.

For each subject group the decrease in sensitivity caused by making the auxiliary field small was calculated for each test flash. For the white test flash the mean decrease was 0.52 and 0.57 log unit for respectively, the patient group and the normal group; for the red test flash the mean decrease was, respectively, 0.17 and 0.21 log unit. For neither of the test flashes was the mean decrease for patients significantly different from that for normals ($t \leq 0.38$, $df = 16$, $p >> 0.05$).

7.3.3 Discussion

The mean threshold for the patient group was significantly increased above that for the normal group for every condition (Fig. 7.3). Further, this mean increase in threshold for patients was essentially the same for all conditions, implying an equal loss in sensitivity of both the opponent-colour system and the luminance system. This lack of specificity in impairment was confirmed by the fact that in both the normal group and the patient group, the decrease in sensitivity to the white test flash produced by making the auxiliary field small was about 0.3 log units larger than the equivalent decrease for the red test flash. Overall, the data indicate that the underlying action spectra of the luminance and opponent-colour systems were the same for patients as for normal subjects. There was, however, a reduction in sensitivity of both systems of about 0.4 log unit in the patient group. Thus, the mean results here for the patient group are compatible with those obtained for patient CB (Fig. 6.4).

To summarize, the data for the patient group do not support the results of previous studies which suggested that either the luminance system or the opponent-colour system is more impaired in MS and ON than the other. The previous studies, cited in Section 1.5.2, varied from each other and from the present work in the experimental methodology used. Fallowfield and

Krauskopf (1984) (using a test stimulus of diameter 2^{o}, with sharp edges, and of total duration 2.2 s, with the temporal profile of a raised cosine) suggested that chromatic function is selectively impaired relative to luminance function. The procedures they used, however, may not have given comparable thresholds for the two functions; thus for chromatic function they measured excitation purity, whereas for luminance function they measured detection threshold. Further, the luminance of the chromatic stimuli was equated by flicker photometry for normal subjects and not for each patient individually. The methodology of Mullen and Plant (1986), who also found a greater impairment of chromatic sensitivity, did not have these complications. The test stimulus consisted of a circular grating, diameter 6.5^{o}. The grating had the spatial profile of a 1-cycle-per-deg sinusoid, and the temporal profile of a 0.5-Hz sinusoid. Luminance contrast sensitivity was measured with monochromatic gratings, and chromatic contrast sensitivity with red/green or blue/yellow gratings which were isoluminant for each eye of each subject.

The test stimuli of the two studies cited above were larger than those used in the present work. Thus a larger retinal area was stimulated, and the variations in size of neurones subserving the retina could explain the different results. In the human optic nerve, foveal neurones are of smaller average diameter than more peripheral neurones (Potts *et al.*, 1972), and in mice infected with Semliki Forest virus, small diameter fibres are preferentially demyelinated (Ikeda and Tansey, 1986). Further, it is believed that, in man, neurones subserving chromatic function in the peripheral retina are of smaller diameter than those subserving luminance function. For stimuli extending into the periphery, therefore, the neurones carrying chromatic information may be more vulnerable to demyelination than those carrying luminance information.

Zisman et al. (1978) and Alvarez et al. (1982) found in some patients that luminance function is more affected than chromatic function is; they used a stimulus of diameter 1^{o}, larger than that used here. TSS curves measured with a 1 deg diameter test field for one patient with MS and ON (Chapter 6, Fig. 6.4), however, revealed a similar non-specific loss in sensitivity to that shown by the group of patients tested here with a smaller stimulus. The difference between the results obtained here, and those of Zisman et al. (1978) and Alvarez et al. (1982) are probably a consequence of the differing time courses of the stimuli; those authors measured sensitivity to 1 Hz flicker (chromatic function) or 25 Hz flicker (luminance function), whereas here a 200 ms flash was used for both functions. In the next chapter, it is suggested that high temporal-frequency response can be impaired in MS regardless of the system mediating that response.

Chapter 8

Temporal processing in MS patients and normal subjects

8 Temporal processing in MS patients and normal subjects*

8.1 Introduction

Data presented in Chapter 7 suggest that in MS or ON or both losses in foveal chromatic sensitivity are not greater than losses in foveal luminance sensitivity when the measures are directly comparable. There are reports of losses in temporal function (see Section 1.4.2), and although static foveal chromatic sensitivity may not be preferentially reduced, it is possible that pathways carrying time-varying chromatic information might be more affected by the disease than those carrying time-varying luminance information. For this reason, it was decided to measure critical flicker frequency (CFF) for a stimulus varying either in luminance content or in chromatic content. Luminance CFF has previously been shown to be lower in MS patients than in normal subjects (Titcombe and Willison, 1961; Daley et al., 1979). CFF depends on the intensity of the stimulus (see Section 1.5.2) yet the abnormal results given by MS patients are not a simple consequence of raised luminance thresholds (Patterson et al., 1981).

This chapter describes two experiments. In Experiment 1 the test stimulus was viewed foveally; in Experiment 2 it was viewed parafoveally. Each experiment was carried out on a separate group of patients and on a separate group of normals individually matched to the patients for age and sex. Both experiments made use of apparatus systems which gave rise to red and green flicker trains which were combined so as to be spatially

* *Experiments described in this chapter were carried out in collaboration with Dr R.J. Mason and Dr R.E. Jones.*

superimposed. The two flicker trains could be presented in antiphase, thus providing primarily chromatic flicker, or in phase, thus providing primarily achromatic, or luminance flicker. The two trains were balanced for luminance content (see below).

8.2 Experiment 1

8.2.1 Methods

The apparatus used in this experiment was Perimeter 1 described in Section 2.3.1. A red and a green LED (calibrations given in Section 2.3.3) provided the stimuli.

Stimuli. The chromatic stimulus consisted of a red and a green flicker train in antiphase (Fig. 2.6). The intensity of the green train was fixed at a luminance of 60 cd.m^{-2} throughout the measurements. The intensity of the red train was equated for luminance to the green by means of a heterochromatic flicker match carried out individually by each subject as described below. To obtain the luminance stimulus the red and green flicker trains used for the chromatic stimulus were presented in-phase (Fig. 2.6). This gave a train of alternating light (yellow) and dark pulses with the same time-averaged spectral and luminance content as the chromatic flicker train. The test stimulus was viewed monocularly and foveally. The end of the fibre optic guide appeared normally as a dark disc in the center of the background field, which was a white square, of side 20 deg visual angle, with luminance 290 cd.m^{-2} and colour temperature 2800K.

Procedure. The subject was instructed to fixate the dark disc, press the push-button switch which initiated a three-second flicker train, and

then report (forced choice) whether or not flicker was seen. The heterochromatic flicker match was carried out by each subject for each eye as follows. The intensity of the red flicker train was varied, and at each intensity the subject reported whether or not flicker was minimal. At a suitable frequency, which varied with the subject, a small range of red intensities gave 'minimum flicker' responses whereas at greater or lesser intensities flicker was seen. Four estimations were made and the mean of the midpoints was calculated to give a value for the red intensity which was equal in luminance to the green intensity. The red intensity was set at this value for both chromatic and luminance CFF estimations. The CFFs were determined by a method of limits in which 3 ascending and 3 descending series of flicker frequencies were used, centred about an approximate threshold determined in a short practise series.

Modified Rayleigh match. In addition to the main experiment, patients 9, 11, and 19 and three normals performed modified Rayleigh matches using the Maxwellian-view system described in Section 2.2.1, except that a chin rest was used to steady the head instead of the usual bite-bar. An annulus, outer diameter 10 deg and inner diameter 2 deg, wavelength 576 nm, and intensity 8.75 log quanta.s^{-1}.deg^{-2}, was provided by channel 3. The annulus surrounded a disc of diameter 2 deg composed of 539 nm light from channel 2 mixed with 651 nm light from channel 1. The experimenter adjusted the neutral-density wedges in channels 1 and 2 until the subject reported that the central disc matched the annulus in colour and brightness. Six such estimations were made and the mean of the ratio of the 651 nm/539 nm intensities was taken. These six subjects also performed the 100-Hue Test.

Subjects. 20 patients took part in the experiment. 14 were female and six were male. Clinical details are given in Table 8.1; the classification

Patient	Age	ON	MS	Duration of Disease (yrs)	Classification
1	54	-	Spinal	30	Progressive Probable
2	32	-	Spinal	2	Suspected
3	27	-	Spinal	4	Clinically Definite
4	59	-	Spinal	3	Progressive Possible
5	28	-	Spinal	3	Early Probable
6	53	-	Spinal	13	Clinically Definite
7	28	-	Brain Stem	1	Suspected
8	63	-	Spinal	33	Progressive Probable
9	54	-	Spinal	4	Early Probable
10	42	-	Spinal	2	Clinically Definite
11	28	+	Spinal	8	Clinically Definite
12	45	+	-	3.5	Optic Neuritis
13	46	+	Spinal	22	Clinically Definite
14	37	+	Spinal	7.5	Clinically Definite
15	50	+	Brain Stem	13	Clinically Definite
16	43	+	Spinal	2	Clinically Definite
17	33	+	Spinal	7	Clinically Definite
18	43	+	-	4	Optic Neuritis
19	48	+	Spinal	5	Clinically Definite
20	29	+	Cerebellar	7	Clinically Definite

Table 8.1 Summary of clinical data for patients who took part in Experiment 1.

criteria used were those of McDonald and Halliday (1977). Eleven of the patients had clinically definite MS, two progressive probable, two early probable, one progressive possible, two suspected, and two had optic neuritis only. For purposes of analysis the whole group of patients were considered firstly as an undifferentiated group, MS group 1, and secondly as two subgroups: subgroup 1A comprised the first ten patients (Table 8.1) with no previous ON and with a mean duration (±1 SEM) of disease of 9.5(±3.8) years; subgroup 1B comprised the remaining ten patients (Table 8.1) with previous episodes of ON and with a mean duration of disease of 7.9(±1.8) years. All patients in subgroup 1A could make the measurements with both eyes, hence results from 20 eyes are available. Four of the patients in subgroup 1B could make measurements with one eye only, giving 16 eyes for which results are available. None of the eyes tested had visual acuity worse than Snellen 6/12 and Near Vision N12. Only two eyes gave abnormal responses to the TCU test: patient 18, R eye, gave 40% tritan errors, and patient 20, L eye, gave 30% protan and 30% deutan errors. No patient reported difficulty in fixation, and none had nystagmus. Twenty healthy subjects, matched individually with the patient group for age and sex, acted as normal controls. These subjects all had normal colour vision according to the TCU test, and covered a range of visual acuity similar to that of the patient group.

Data analysis. Raw flicker data were analyzed as described in Section 7.2.1. For each CFF, a mean and standard error were then calculated over all eyes for each patient group and the normal group. Significance levels of differences between groups were calculated using one-tailed t-tests.

Least-squares regression lines were fitted for chromatic CFF plotted against luminance CFF, for each patient group and the normal group. Correlation coefficients were calculated for chromatic CFF with luminance

CFF, chromatic CFF with age, and luminance CFF with age.

8.2.2 Results

The mean results (±1 SEM) for each group are given in Table 8.2. The superscripts indicate levels of significance for differences between groups. The undifferentiated MS group 1 gave a reduced mean CFF when compared with the normals for both chromatic CFF ($p < 0.05$) and luminance CFF ($p < 0.001$). Mean CFFs for subgroup 1A (without previous ON) were not significantly different from those for the normals, though they were slightly lower. Subgroup 1B (with previous ON) gave a highly significantly reduced mean luminance CFF when compared with that of the normals ($p < 0.0005$); it was also significantly different from that of subgroup 1A ($p < 0.01$). Additionally, subgroup 1B had a significantly reduced chromatic CFF relative to the normals ($p < 0.01$) and subgroup 1A ($p < 0.05$).

	Mean threshold in Hz	
	Luminance CFF	Chromatic CFF
Normal Group	31.6(±0.8)	20.5(±0.9)
MS Group 1	27.5(±1.0)[1]	17.9(±0.7)[3]
Subgroup 1A	29.7(±0.8)	19.1(±0.8)
Subgroup 1B	24.7(±1.8)[2]	16.4(±1.2)[4]

Table 8.2 Experiment 1: means (±SEM) for normal group and patient groups. MS group 1 comprises all patients; subgroup 1A comprises those patients without previous ON; subgroup 1B comprises those patients with previous ON. Levels of significance for differences between groups are indicated by the superscripts thus:

	MS Group 1 v. Normals	Subgroup 1B v. Normals	Subgroup 1B v. Subgroup 1A
1	$p < 0.001$	-	-
2		$p < 0.0005$	$p < 0.01$
3	$p < 0.05$	-	-
4	-	$p < 0.01$	$p < 0.05$

More detailed analysis of the CFF data is given in Figs. 8.1(a)-(d) where chromatic CFF is plotted against luminance CFF for, respectively, the normal group, MS group 1, subgroup 1A, and subgroup 1B. Open circles indicate those eyes which have had previous attacks of ON. Evidently, chromatic CFF and luminance CFF are linearly related for both normal and patient groups. The correlation coefficients for the normal group, MS group 1, subgroup 1A, and subgroup 1B are 0.89, 0.78, 0.43, and 0.92 respectively. The main difference between the normal group and each of the patient groups lies in the gradients of the regression lines which are fitted to the data. For the normal group the regression line has a gradient of 1.063, whereas the regression lines for MS group 1, subgroup 1A, and subgroup 1B have gradients of, respectively, 0.555, 0.416, and 0.607; the difference between the gradient for the normal group and the gradient for each of the patient groups reaches significance (each $p < 0.005$).

Correlation coefficients were also calculated for luminance CFF with age of subject, and chromatic CFF with age of subject, for patients and normals. MS group 1 gave very low coefficients: 0.09 for chromatic CFF with age; 0.06 for luminance CFF with age. In contrast, the normal group gave highly significant (each $p < 0.001$) coefficients of 0.80 and 0.81 respectively. Other possible causes for the difference between the gradients, for example, Snellen acuity and red intensity obtained in the heterochromatic flicker match, did not show significant correlation coefficients with either CFF. In the Rayleigh match, the three patients required more red than did the normal subjects, but only for patient 11 was the difference of the red/green ratio from the normal ratio significant ($p < 0.05$). The error score on the 100-Hue test for patients 9, 11, and 19 was 138, 156, and 109 respectively, with no obvious polarity.

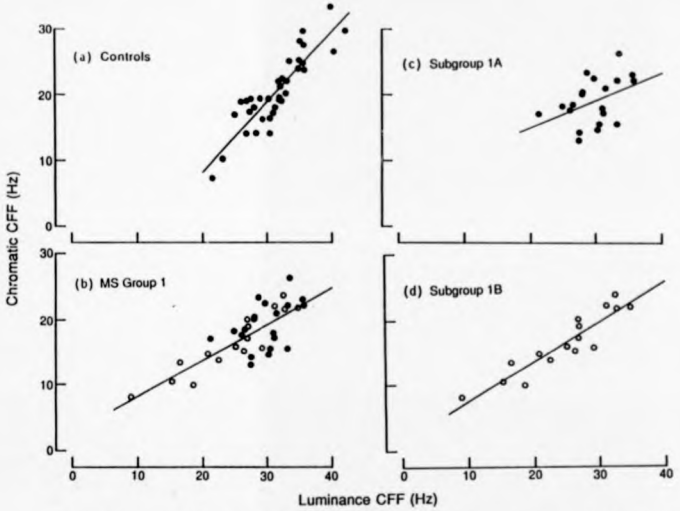


Figure 8.1 Chromatic CFF plotted against luminance CFF (Experiment 1). The straight lines are least-squares linear fits to the data. (a) shows the CFF plot for normal control subjects; (b) the CFF plot for all MS patients, MS group 1, open symbols indicating results from patients with previous ON; (c) the CFF plot for patients without a history of ON, subgroup 1A; (d) the CFF plot for patients with a history of ON, subgroup 1B.

8.3 Experiment 2

It is possible that there may be a differential impairment of fibres leading from parafoveal receptors compared with those leading from foveal receptors (see Section 7.3.3). For this reason, measurements of chromatic CFF and luminance CFF similar to those described above were carried out for parafoveal retinal sites.

8.3.1 Methods

The apparatus used was Perimeter 2 described in Section 2.3.1. The chromatic and luminance stimuli were essentially as described above for Experiment 1, except that, instead of LEDs, an incandescent light source and gelatine filters were employed (calibrations given in Section 2.3.3).

Stimuli. Luminance of the red flicker train was fixed throughout at 132 $cd.m^{-2}$. The test stimulus was presented monocularly at one of four locations of eccentricity 2.5 deg and azimuth 45 deg to the horizontal. The circular background field was white, of diameter 20 deg, with luminance 160 $cd.m^{-2}$ and colour temperature 3060K. A central target in the form of a white annulus, of diameter 35 min of arc, was provided to aid fixation.

Procedure. For this experiment, estimations were made at each of the four retinal sites for one eye only of each subject. The heterochromatic flicker match was as described above for Experiment 1, except that the intensity of the green flicker train was varied so as to equate its luminance to that of the red flicker train. Data for chromatic and luminance CFFs were then collected by the randomized block method described in Section 2.3.4.

Subjects. Seven patients took part in this experiment. Each made measurements for the four parafoveal sites, giving 28 sets of measurements in all. All were female. Patients were classified according to the criteria of McDonald and Halliday (1977). Clinical details are given in Table 8.3. Only two patients had suffered more than one relapse and only one patient (No.3, Table 8.3) had active progressive demyelination. Three patients had clinical evidence of past ON. None of the patients had advanced disease, and as a whole they were representative of relatively benign MS (McAlpine et al., 1965). For purposes of analysis the whole group of patients were considered first as an undifferentiated group, MS group 2, and second as two subgroups: subgroup 2A comprised the first four patients (Table 8.3) with no previous visual symptoms and with a mean duration ($\pm$1 SEM) of disease of 2.1($\pm$1.0) years; subgroup 2B comprised the remaining three patients (Table 8.3) with previous episodes of ON and a mean duration of disease of 6.0($\pm$2.1) years. Seven healthy subjects, matched individually for age and sex with the patient group, acted as normal controls. No subject had visual acuity worse than Snellen 6/9 and Near Vision N12. All had normal colour vision as classified with the TCU test. No patient had nystagmus.

Data analysis was as for Experiment 1.

8.3.2 Results

Table 8.4 shows mean results with standard errors in parentheses. Levels of significance for differences between groups are indicated by superscripts. The undifferentiated MS group 2 gave a marginally reduced mean luminance CFF when compared with the normal group ($p < 0.05$). Subgroup 2B gave a highly significantly reduced mean luminance CFF relative to both the normal group and subgroup 2A ($p < 0.005$). There were no

Patient	Age	ON	MS	Duration of Disease (yrs)	Classification
1	28	-	Spinal	1	Early Probable
2	30	-	Spinal, Brain Stem, Cerebelar	5	Early Probable
3	47	-	Spinal	2	Progressive Probable
4	48	-	Spinal, Cerebellar	0.5	Progressive Possible
5	34	+	Spinal, Sensory	10	Early Probable
6	37	+	Spinal	3	Early Probable
7	42	+	Spinal	5	Clinically Definite

Table 8.3 Summary of clinical data for patients who took part in Experiment 2.

	Mean threshold in Hz	
	Luminance CFF	Chromatic CFF
Normal Group	28.8(±0.7)	15.5(±0.8)
MS Group 2	26.4(±0.9)[1]	14.1(±0.8)
Subgroup 2A	28.5(±1.0)	14.4(±1.2)
Subgroup 2B	23.5(±1.4)[2]	13.9(±0.9)

Table 8.4 Experiment 2: means (±SEM) for normal group and patient groups. MS group 2 comprises all patients; subgroup 2A comprises those patients without previous ON; subgroup 2B comprises those patients with previous ON. Levels of significance for differences between groups are indicated by the superscripts thus:

	MS Group 2 v. Normals	Subgroup 2B v. Normals	Subgroup 2B v. Subgroup 2A
1	$p < 0.05$	-	-
2		$p < 0.005$	$p < 0.005$

significant differences between the groups for mean chromatic CFF.

In Figs. 8.2(a)-(d) chromatic CFF is plotted against luminance CFF, as described for Experiment 1, for the normal group and each of the patient groups, and the least-squares regression lines are shown. For the normal group (Fig. 8.2(a)) the correlation coefficient was 0.71. For the patient groups (Figs. 8.2(b)-(d)) the correlation coefficients were lower : 0.24, 0.35, and 0.22 for the undifferentiated MS group 2, subgroup 2A, and subgroup 2B, respectively. Nonetheless, there was an evident difference between the gradient for the normal group and the gradient for each of the patient groups: 1.02 for the normal group versus 0.17, 0.51, and 0.11 for the undifferentiated MS group 2, subgroup 2A, and subgroup 2B, respectively. This difference reached significance for the undifferentiated MS group 2 and for subgroup 2B (each $p < 0.005$).

8.4 Discussion

8.4.1 Luminance CFF

Patients with MS have previously been reported as having abnormally lowered CFF for foveal luminance flicker (Titcombe and Willison, 1961; Daley et al., 1979). The results of Experiment 1 agree with the results of those studies: the difference between the normal group and MS group 1 was highly significant ($p < 0.001$). The results of Experiment 2 extend the fact to luminance CFF determined for parafoveal sites: the difference between the normals and MS group 2 was also significant ($p < 0.05$). A direct comparison cannot, however, be made easily between the absolute values of CFF for the different regions of the retina (i.e. foveal or parafoveal) at which measurements were made in the two experiments. First, the stimulus conditions were slightly different in each experiment.

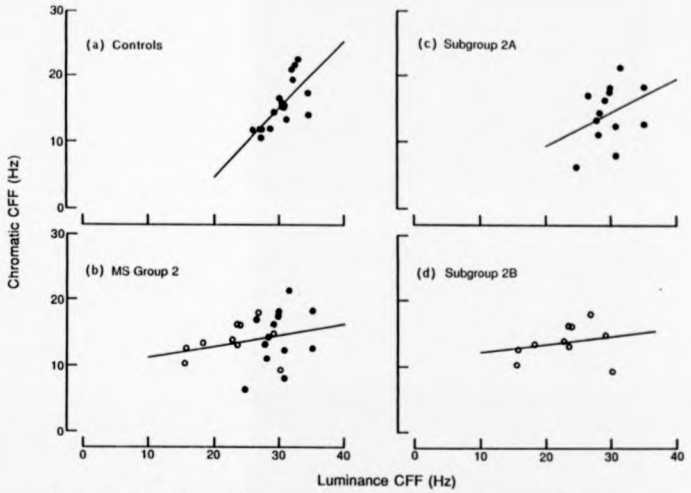


Figure 8.2 Chromatic CFF plotted against luminance CFF (Experiment 2). The straight lines are least-squares linear fits to the data. (a) shows the CFF plot for normal control subjects; (b) the CFF plot for all MS patients, MS group 2, open symbols indicating results from patients with previous ON; (c) the CFF plot for patients without a history of ON, subgroup 2A; (d) the CFF plot for patients with a history of ON, subgroup 2B.

Second, the patient groups were dissimilar: for example, MS group 1, on the whole, had more advanced MS (10/20 of MS group 1 had clinically definite MS, Table 8.1, compared with 1/7 of MS group 2, Table 8.3).

An interesting difference emerges when the MS groups are divided into those with and those without previous ON. Thus subgroups 1B and 2B (both with previous ON) show a large reduction in luminance CFF relative to normal (Table 8.2, $p < 0.0005$, and Table 8.4, $p < 0.005$) whereas subgroups 1A and 2A (without previous ON) show only small reductions in luminance CFF which are not significantly different from normal. Indeed, there are significant differences between both subgroups 1A and 1B ($p < 0.01$), and 2A and 2B ($p < 0.005$). This finding is consistent with the results of Titcombe and Willison (1961) that a higher percentage of patients with previous RBN gave low CFF values than did those without previous RBN. Daley et al. (1979), however, found no clear differential effect of previous visual disturbance.

8.4.2 Chromatic CFF

It appears that chromatic CFF has not previously been measured in patients with MS. In the present experiment it was found that foveal chromatic CFF was significantly different from normal for the undifferentiated MS group 1 ($p < 0.05$). There was no significant reduction from normal, however, for parafoveal chromatic CFF. Possible explanations are as follows.

(1) Those fibres which mediate detection of chromatic information when it is presented to parafoveal receptors might be less susceptible to demyelination, or the damage caused by demyelination, than both the corresponding foveal fibres and those fibres, parafoveal and foveal, which

mediate detection of luminance information (Section 7.3.3).

(2) As discussed earlier, the two MS groups were dissimilar. In particular, the patients in MS group 1, who had more advanced disease than those in MS group 2, might be expected to show a greater degree of impairment; indeed, over all measures, those patients who took part in Experiment 1 showed more significant differences, with a higher level of significance, than did those who took part in Experiment 2.

(3) As also mentioned previously, the experimental conditions employed for the two retinal regions were dissimilar.

(4) Mean chromatic CFF for normals was lower for the parafovea (15.5 Hz) than for the fovea (20.5 Hz). This difference, 5 Hz, was both proportionately and absolutely greater than that for luminance CFF (with a mean difference for normals of 2.8 Hz). The nature of this normal reduction would need to be assessed using a range of test-field size (cf Kuyk, 1982). In the present study, the fact that chromatic CFF measured at the fovea was higher for normals than that measured in the parafovea may be the reason for chromatic CFF being more reduced at the fovea than in the parafovea in MS patients. As will be argued below, it seems that the higher the CFF normally the greater will be the effect of demyelination.

Dividing MS group 1 into those with and those without ON revealed a very similar effect for chromatic CFF to that for luminance CFF: subgroup 1A (without previous ON) showed no significant difference from normal, whereas Subgroup 1B (with previous ON) gave a result which is significantly different both from the normals ($p < 0.01$) and from subgroup 1A ($p < 0.05$). Dividing MS group 2 likewise, however, did not reveal a significant reduction of chromatic CFF for subgroup 2B.

8.4.3 Relationship between the CFFs

It is apparent in Figs. 8.1(a)-(d) and 8.2(a)-(d) that chromatic CFF is linearly related to luminance CFF for both normal subjects and MS patients. It has been shown above that for normals this relationship depends on a correlation of each of the CFFs with age (each $p < 0.001$). A dependency of luminance CFF on age has been reported previously (McFarland et al., 1958), and the present results show that it also holds for chromatic CFF. For MS patients, however, the relationship between the CFFs does not depend on age; for example, for MS group 1 the correlation between age and each of the CFFs were less than 0.1.

It has been shown above that MS patients obtain lower CFF than normal, and this must be an effect of demyelination. The greater the degree of demyelination then the greater the abnormality of CFF, or, indeed, of any visual function (see, for example, Galvin et al., 1977). Certainly, the occurrence of previous ON seems to lead to greater abnormality. Degree of demyelination is not linked to age and, therefore, over a group of patients with varying degrees of demyelination the effect of age on CFF would be suppressed. That the CFFs remain correlated must be the result of each of them being reduced in a related manner.

The original aim of these experiments was to determine whether fibres carrying time-varying chromatic information are likely to be more impaired by demyelination than those carrying time-varying luminance information. A preferential impairment seems not to be the case. The mean results (Tables 8.2 and 8.4) show that luminance CFF was more reduced than chromatic CFF. This is confirmed by Figs. 8.1(a)-(d) and 8.2(a)-(d). If CFFs for patients had been equally reduced then the gradient of the regression line would have been the same as that for normals, though the

position of the data would have been shifted relative to the x and y axes. If chromatic CFF had been more reduced than luminance CFF, then the gradient would have changed, but it would have become steeper. In fact the gradients for the patient groups are shallower than those for the normals, indicating that chromatic CFF is less reduced than is luminance CFF.

The fact that luminance CFF is more reduced than chromatic CFF need not imply a preferential impairment of those fibres carrying time-varying luminance information. Work on animal models of demyelination (McDonald and Sears, 1970; Halliday and McDonald, 1977; Tansey and Ikeda, 1986) have shown that demyelinated nerve fibres show an impairment in the ability to transmit high frequency impulses, in addition to an intermittent conduction block. Demyelination may, therefore, be thought to act as a low pass filter. This would cause more attenuation of high frequency impulses than of low frequency impulses, irrespective of their functional origin. Thus luminance CFF, simply because it is higher in the normal than is chromatic CFF, would be most reduced.

As indicated above, such an explanation could underlie the apparent normality of parafoveal chromatic CFF in MS patients. In normals there is a 5 Hz difference between the fovea and the parafovea for chromatic CFF; the relatively low parafoveal CFF might, therefore, not show significant impairment in patients. A method of testing this last point would be to employ stimulus conditions which would result in higher parafoveal chromatic CFF in normals. If it could be raised to around 20 Hz (the present mean foveal chromatic CFF for normals) then one might expect it to be reduced when measured for MS patients.

Chapter 9

Conclusions

9 Conclusions

This chapter reviews the main findings of this thesis and considers their implications.

9.1 Isolation of the opponent-colour system in normal subjects

It was originally hypothesized that the introduction of an auxiliary field spatially coincident with the test field would prove effective in isolating the opponent-colour system at increment threshold. In measures of test spectral sensitivity (Section 3.2) use of this auxiliary field did result in an increased depth of the trough at about 580 nm relative to that obtained on the large auxiliary field, by 0.34 to 0.47 log units. Evidence obtained by King-Smith and Carden (1976) for this trough being characteristic of the opponent-colour action spectrum was given in Section 3.1.1. Thresholds for simple-detection and colour-discrimination criteria were shown in Section 3.3 for wavelengths spanning the region of the trough and for a range of auxiliary-field luminances. For simple detection the trough in spectral sensitivity at about 580 nm progressively deepened with increasing auxiliary-field luminance and reached its lowest values at auxiliary-field luminances of 3000 to 10,000 Td, where the curves were very close to those obtained for colour discrimination in the same experiment. In contrast, for colour discrimination, the trough in spectral sensitivity remained fairly stable over all luminances of the auxiliary field. The similarity of detection and discrimination troughs at auxiliary-field luminances of 3000 Td or higher provided strong support for the hypothesis that the small auxiliary field secured isolation of the opponent-colour system at simple-detection threshold. There is a residual difference, even at 3000 Td and above, between thresholds for colour discrimination and

simple detection at around 580 nm. It is possible that this difference could be eliminated by making the white auxiliary field temporally coincident as well as spatially coincident with the test field; that is by combining the techniques of King-Smith and Carden (1976), Foster (1981), and Finkelstein and Hood (1981). For practical purposes, however, isolation was sufficient with the paradigm used here.

Chapter 4 described use of the small-auxiliary-field paradigm in measures of FSS. The field curves of the long- and medium-wavelength sensitive mechanisms were spectrally sharpened in a manner similar to that reported by Foster (1981) who used monochromatic auxiliary fields. Chapter 5 reported an investigation of the similarity of the test spectral sensitivity curve with the upper envelope of the field spectral sensitivity curves, when both were obtained on the small white auxiliary field. It was suggested that this correspondence in shape might result from the action of unitary opponent-colour mechanisms, with a spectral sensitivity that was qualitatively the same for direct measures and adaptational measures of sensitivity. This hypothesis was assessed by means of varying the chromaticity of the auxiliary field. It was shown that the correspondence of the test curve and the field curves persisted, both varying in the same manner with the adapting field. A further assessment of unitary mechanisms underlying the two types of curve could be made by measuring both for a range of auxiliary-field luminance. The increasing depth of trough in the test spectral sensitivity curve, with increase in auxiliary-field luminance, should be accompanied by an increase in the extent of sharpening in the L and M field curves.

Other paradigms have been used to improve isolation of the opponent-colour system in measures of test spectral sensitivity (studies cited in Section 3.2.3). The test action spectra obtained with these other

paradigms appear similar to those obtained here with the small white auxiliary field. The efficacy of each paradigm could be assessed by comparing test spectral sensitivities for the paradigms using the same subjects. The small-auxiliary-field paradigm has an advantage over the other paradigms in that the stimuli can be restricted to a small retinal region so that detection is mediated by a fairly homogeneous group of nerve fibres.

9.2 Opponent-processing in subjects with inherited and acquired deficiencies

In Chapter 6 the small-auxiliary-field paradigm was applied to the assessment of deficiencies in opponent-colour processing. Test spectral sensitivity was measured for a protanope and a deuteranope. The suggestion made by Hurvich and Jameson (1962) that dichromats lack the 'red-green' opponent pathway but possess three photopigments was neither refuted nor confirmed by the results obtained here. It was suggested, however, that the possession of only the L- or the M-sensitive photopigment would, in itself, result in severely spectrally modified or functionally absent 'L-M' pathways; it did not seem necessary to postulate a specific neuroanatomical deficiency in these pathways. Further, it was suggested that the fall in sensitivity to middle-to-long wavelengths in dichromats, produced by making the auxiliary field spatially coincident with the test field, indicates normal neural connections in the dichromat's 'L+M' pathways.

The small-auxiliary-field paradigm was also applied in the investigation of post-receptoral processing in patients with MS or ON (Section 7.3). No differential impairment in chromatic and luminance function was found. This result contrasts with the results of Mullen and Plant (1986) and Fallowfield and Krauskopf (1984) who suggested that

chromatic function was the more impaired. Methodological differences could underly the contradictory results; in particular, the different test-stimulus sizes could have resulted in the selection of different groups of fibres, which in turn may have been differentially impaired by demyelination. Presenting the stimuli to peripheral sites would reveal whether fibres subserving chromatic function in the periphery are preferentially susceptible to the effects of demyelination. For the more eccentric sites, the confounding effect of stimulus size would need to be considered (see Kuyk, 1982; Krastel et al., 1983).

The results obtained in Section 7.3 also contradicted those of King-Smith and his colleagues, who found a differential impairment in luminance function. The test stimulus used by King-Smith and his colleagues to measure luminance function was flickering at 25 Hz, whereas in the present experiments a 200 ms flash was used. It was shown in Chapter 8 that temporal-frequency response may be impaired in patients regardless of the system mediating detection.

9.3 Temporal processing in multiple sclerosis and optic neuritis

The possibility that demyelination might affect pathways carrying time-varying chromatic information more than those carrying time-varying luminance information was investigated in Chapter 8. Analysis of the reduction in chromatic and luminance CFF in patients seemed to show, however, that luminance function was the more impaired. This apparent preferential impairment of the pathways carrying time-varying luminance information was attributed to a general impairment in the ability to transmit high-frequency impulses, consistent with the results of animal models of demyelination.

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